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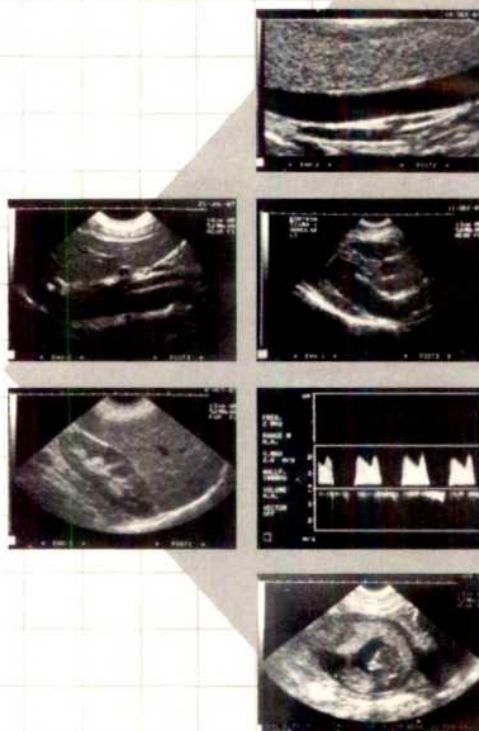
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Review article

The production of chromosome structural changes by radiation: an update of Lea (1946), Chapter VI

By John R. K. Savage, DSc

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(Received November 1988 and in revised form December 1988)

No one can read the papers of the early radiation biologists without being impressed, almost awed, by the depth and thoroughness with which they tackled their topics. Every ounce of information is extracted from the results, every possible avenue of interpretation and implication is explored.

Douglas Lea's *Actions of Radiations on Living Cells* (first edition, 1946) is a classic example. It is a work that has had a profound influence on radiobiology and is still widely quoted today.

Many of Lea's fundamental concepts were based on the qualitative and quantitative production of visible chromosome structural changes, particularly in the plant *Tradescantia*. In accord with Sherlock Holmes' aphorism,* before theorizing, he summarizes and evaluates in Chapter VI the experimental facts. In the intervening years an enormous amount of radiation cytogenetics has been done and it is fair to ask the question "How stands the foundation?". I do not intend to review the whole field in this paper but, using the same section headings Lea used, to comment on and update, in the light of more recent work, some of the statements and ideas he developed. The format of the comments presupposes that the reader has a copy of Lea (1946) to hand.†

Preamble

Before looking at the individual sections, it will be helpful to describe some of the conceptual changes that have occurred since Lea wrote his book and that influence current thinking.

Undoubtedly the most important of these concerns chromosome architecture and the key role of DNA in it. In Lea's day, nucleic (or thymonucleic) acid was regarded as an "adduct", adsorbed to the chromosome

during its condensation process (p. 128) and its property of polymerization was believed to assist the contraction/coiling of the chromosome threads ("chromonemata"). Hence, regions could be "starved" of, or have "excess charge" of, nucleic acid, and depolymerization could produce surface stickiness (Darlington & La Cour, 1945, and see pp. 135 and 193). We now believe DNA to be an integral part of the chromosome, each chromatid having one giant molecule continuous from end to end responsible for its continuity. The contraction/condensation is brought about by histone proteins, some of which are also an integral part of the chromosome (Lima de Faria, 1983). Thus, not only is the structure radically different, but also the dimension of a "chromonema" [$\sim 0.1 \mu\text{m}$ (p. 271) versus $\sim 2.5 \text{ nm}$].

A second conceptual change concerns the complexity of the interphase nucleus within which the primary events of "breakage" and "rejoining" take place. It is apparent from the discussions that the early theorizers thought in terms of a bag of broken chromosomes, whose ends were free to flap around and find alternative partners with which to rejoin. We now know that chromosomes occupy localized domains, that there is an intranuclear cage or scaffold that limits movement, and that most of the DNA is "splinted" with protein and so restricted in both access and exchange potential. Moreover, some DNA is "spun out" and closely associated with the nuclear envelope (and possibly with DNA from other chromosomes) for functional purposes (Nelson et al, 1986). It may be that only this "wandering" DNA constitutes the aberration-forming component of the chromosomes.

A third factor springs from chromosome architecture, namely that there are orders of magnitude difference between the "target" and the microscopically observed aberrations. Early workers equated the two. In fact, enormous lengths of DNA are involved in the construction of a visible chromosome. A scale model in 0.8 mm diameter cotton of the unduplicated $\sim 6 \text{ pg}$ of DNA in a human cell would require $\sim 608 \text{ km}$ and there would be five times that amount in a haploid

*"It is a capital mistake to theorise before one has data", Sherlock Holmes in *A Scandal in Bohemia* by A. Conan Doyle.

†Textual quotations and page numbers are taken from the first edition (1946) and Appendix II of the second edition (1955) by kind permission of the publishers, Cambridge University Press.

Tradescantia pollen grain which Lea and his colleagues used! Consequently, it is advisable now to distinguish carefully between *induction*, the step at the molecular level that leads to an aberration, and *production*, the visible manifestation of a recognizable structural change seen at mitosis. It is obvious that modification and disguise during the packing/condensation process will negate any 1:1 relationship. Couple this with the fact that many significant structural changes may occur at levels well below that which can be seen with the light microscope and it will be realized that we are only collecting a small proportion of the actual events that have occurred. It follows that, when theorizing, the jump from the visible to the molecular and *vice versa* must always be made with extreme caution. Nevertheless, recent studies combining techniques that relate double-strand DNA break frequencies with aberrations visualized and measured in prematurely condensed interphase chromosomes (Cornforth & Bedford, 1983; Iliakis et al, 1987) suggest that the visible/molecular discrepancies may not be as large as we might anticipate.

Fourthly, the concepts of "repair". The dominating thought of these early workers was "What happens to the broken ends?" Is it *restitution* (restoration of the original configuration) or *rejoining* (joining with another break close in space and time), or does it remain open? The idea that the process of repairing the damage may itself lead to aberration formation is absent. Such concepts could only come with the realization that many chemical agents are able to produce qualitatively identical structural chromosome changes, and the mechanism for their formation could not be accommodated within the ideas of the fate of primary breaks. Having identified the principal target as the DNA, we now know that cells have a large number of inbuilt repair processes to deal with damage in it. Many cell types, including some inherited syndromes in man, have defects in these repair mechanisms and as a consequence are extra sensitive to the induction of aberrations by certain agents. Of particular interest are those which show excessive sensitivity to radiation [e.g. ataxia telangiectasia (Bridges & Harnden, 1982)] for these caution us against a simplistic approach to aberration production even by ionizing radiation.

In addition to such conceptual differences, there have been many important technical developments that have aided understanding, some of which will be discussed in appropriate sections below.

Experimental materials (pp. 189–192)

"For the detailed study of structural changes it is necessary to use nuclei in which the chromosomes are large and few in number" (p. 189). There were only about a dozen or so genera which fulfilled these criteria and most of them were plants, in particular *Tradescantia*. Mammalian cytogenetics was almost non-existent. Lea argued that "in view of the almost complete universality of the chromosome mechanism ... the main conclusions ... will be of wider

application" (p. 189), a prediction amply vindicated. Apart from the discovery of new phenomena, extensive studies of new genera (including humans) have not required drastic revision of these early findings. The emphasis on few chromosomes, whilst having observational advantages, turns out to have unexpected quantitative disadvantages (Savage, 1970), which will be discussed later. The materials Lea and early workers used were all intact ("*in vivo*") cell systems (anthers, root meristems, salivary glands). They were regarded as relatively simple and homogeneous, but have since turned out to be rather complex, and at times beset with cell kinetic problems, which makes interpretation difficult (Clowes, 1967; Mephem & Lane, 1969; Van't Hof & Kovacs, 1971; Wigglesworth, 1975; Savage, 1975).

The advent of mammalian cell tissue culture has opened the possibility of *in vitro* experimentation and better control of cell development. Although cell kinetic complexities are still present, a large number of methods for marking positions of cells within the cycle have been developed to help with interpretation, and some of these can also be applied *in vivo*.

The banded polytene salivary gland chromosomes of *Drosophila* larvae provided an opportunity to analyse (transmitted) chromosome damage in considerable detail, albeit with the problems of extreme cell selection to complicate interpretation (p. 191). Similar "banding", at a lower level of resolution, can now be produced regularly in mammalian somatic chromosomes (ISCN, 1978, 1981, 1985) and has been used to study several aspects of aberration formation both experimentally and clinically.

Structural changes and physiological changes in chromosomes (pp. 192–197)

Lea regarded the chromosome as a specific target for radiation and recognized two broad responses that he defines on p. 196. "Physiological effects ... exhibited by the cells already in division at the time of irradiation and ... structural changes ... exhibited by the cells which enter division after the expiration of the period of reduced mitotic activity which follows irradiation".

Both are always found, but the extent of the former is very species dependent, and appears to be more obvious in plants. Its prevalence may be related to the duration of the post-replication phase (G_2).

The suggested explanation of physiological effects as "a general change in surface properties" and "fluid unpolymers nucleic acid" producing "surface stickiness" (p. 193) is no longer tenable from our understanding of chromosome structure. Later studies, particularly of the side-arm bridges seen at anaphase (illustrated in Plate IV), led to the idea that these effects arose from sub-chromatid or half-chromatid changes (of which Lea was not unaware, see p. 201) consonant with the widely held view that the chromosome had a multi-stranded structure (Evans, 1962; Wolff, 1969). Current views, however, favour a single-strand ("*unineme*") model, and the apparent sub-chromatid exchange will

therefore arise from ordinary exchange produced in an already condensed structure (Kihlman, 1971). Furthermore, we now know that there is a very critical period late in G₂ when potential aberration yields can be modified by a variety of agents, particularly DNA synthesis inhibitors (Kihlman et al, 1982; Moore et al, 1988) and radiation at or after this stage could well be responsible for these "physiological" effects. There are also many proteins and enzymes associated with condensed chromosomes, effects on which can also lead to "stickiness" (Gaulden, 1987).

Much more localized "stickiness" is sometimes seen associated with conventional structural aberrations (Moore, 1980).

Types of structural change (pp. 197–211)

In fundamental work, accurate identification and classification of structural changes is essential and these early workers developed a nomenclature that is still widely used today.

The criteria used may be summarized under four headings:

1. *Duplication status*. "Chromosome" versus "chromatid". The former are produced in "unsplit" (pre-duplicated, pre-S) chromosomes so that the breaks always affect both chromatids at the same locus. The latter are produced in "split" (duplicated, post-S) chromosomes and usually affect only one of the chromatids at any one locus.

2. *Disposition of breaks*. When two or more breaks are involved, both may be in the same chromosome ("intrachanges") or in different chromosomes ("interchanges"). In later papers, Lea and other workers found it useful to include chromosome arms ("intra-arm" and "inter-arm") for intrachanges.

3. *Rejoining symmetry*. "Asymmetrical" (A) are those aberrations that always produce acentric fragments and sometimes mechanical problems at anaphase. "Symmetrical" (S) aberrations do neither, unless incomplete rejoining is present.

4. *Completeness*. Some types of aberration show incomplete rejoining and this can be specified. For A-type changes, incomplete ends can be located as proximal, p, or distal, d, in relation to the centromere.

More details, diagrams and full descriptions of aberration types can be found in many publications (Evans, 1962; Savage, 1975, 1976).

Lea illustrates most of the common types of "unsplit" (Fig. 30, p. 194) and "split" (Fig. 31, p. 195) aberrations together with their anaphase segregation patterns. In retrospect, it is interesting to note that in the interests of simplicity, most of the chromatid intra-arm intrachanges (see below, Fig. 1) are not included, although he was fully aware of their existence (p. 207). It was this category that was later to form the basis of the main line of attack against the Lea/Sax "breakage-first" hypothesis.

In the intervening years, apart from the controversial "sub-chromatid" aberrations mentioned above, and the

more complex multilesion or insertion intrachanges (Fox, 1967; Savage, 1976, 1986), which are very frequent with chemical clastogens, no new types of aberration have been discovered. A possible exception may be heritable fragile sites (Sutherland, 1983), which appear to be S-dependent structural changes with very variable expression (Savage & Fitchett, 1988).

Since one of his primary criteria was duplication status, Lea devotes some discussion to the "time of split" (pp. 197–199) as determined by the transition from chromatid to chromosome-type aberrations when the sampling time is increased sequentially after radiation. He concluded (using data from Sax) that for *Tradescantia* microspores, it was "between 26 and 32 h prior to metaphase". This was the first unequivocal demonstration of a discrete replication phase within interphase. The use of radioactive tracers, first applied by Howard and Pelc (1951), has since defined the familiar S-phase and its preceding and following "Gap 1" and "Gap 2", respectively, thus providing the basis for a routine cell cycle analysis.

These early workers tended to think of the splitting process like a zip fastener, and from the discussion here, clearly considered it a very rapid process such that whole nuclei had either split or unsplit chromosomes. Very few cells with mixed chromosome and chromatid aberrations are observed.

The use of the thymidine analogue, bromodeoxyuridine, coupled with differential staining has shown the replication process to be much more complex, and closely related to the ordered chromosome architecture manifested by banding. Each chromosome has a precise programme, replicating its bands in a specific sequence (Dutrillaux et al, 1976). The whole process appears to take most of the S-phase, which is ~7 h in mammals, and the sequence may be used to provide a fine cell cycle analysis (Savage et al, 1984). Thus we should think of cells having "split" chromosome regions rather than a split/unsplit status for whole cells.

Chromosome breaks (pp. 199–201)

In all his arguments and calculations, Lea regarded the simple "break" (terminal deletion) as the primary event, "the simplest type of aberration" (p. 199). One of three fates awaited it: (a) to remain as an open, unrejoined break with the acentric fragment being lost at subsequent divisions with probable death of the deficient cell, (b) to "restitute" or "heal", restoring the original chromosome, or (c) to "rejoin" with another broken end (close in space and time) within the nucleus forming the various types of intra- or interchange aberrations.

This, in essence, is the "breakage-first" hypothesis (Stadler, 1932). The alternative hypothesis, then current, that contact between non-homologous chromosome threads was a necessary prerequisite for aberration formation, and that exchanges arose from unorthodox crossing over ["contact-first" (Serebrovsky, 1929)], was felt to be demolished by the quantitative dose-response

and radiation intensity effect findings (Sax, 1940). However, in the light of aberration formation by chemicals, and our understanding of the complex molecular repair mechanisms in the nucleus, the distinction between these opposing ideas does not now appear so clear cut as it did then.

True terminal deletions are much rarer than was once thought, which reflects the generally low level of incomplete aberrations in pre-S cells. Even with the most critical analysis it is frequently impossible to distinguish between them and interstitial deletions, particularly when smaller mammalian chromosomes are used.

Lea claimed (p. 200) that in some materials (but not in *Tradescantia*) the broken ends of the chromosomes could fuse with each other upon duplication to give sister-chromatid reunion (SU) and consequent bridging at anaphase. He includes this possibility in Fig. 30 (A4 and A6). This was challenged by several workers (Thoday, 1953) and the general consensus today is that true pre-S terminal deletions never show SU.

Chromatid breaks (p. 201)

"The chromatid breaks vary in distinctness, sometimes appearing only as *achromatic lesions* in the chromatid and are not easy to score with accuracy" (p. 201). Here Lea alludes to a problem which has been a perpetual area of heated controversy and is still with us today: When is a break not a break?

Achromatic lesions (or "gaps" as they are sometimes called) are very rare when pre-split chromosomes are irradiated but very common in post-split chromosomes, particularly those irradiated close to division. Most workers now admit that gaps are not breaks (or "discontinuities", to use a more precise term); the problem lies in making the distinction when scoring. The cleanest test—Does it produce an acentric fragment at anaphase? (Revell, 1959)—is not a practical proposition in most experiments. When applied, it indicates that true discontinuities are relatively rare, but considerable differences can exist between different organisms. Another approach, using differential ("harlequin") staining of chromatids, led Heddle and Bodycote (1970) to conclude that some lesions that would be scored as gaps are, in fact, true breaks.

The generally accepted criterion for metaphase scoring is to require a break to show a clear dislocation or displacement between the broken ends (Savage, 1975, 1976). However, when electron microscope studies are applied to the problem, even this criterion is found unreliable, and continuity at the 30 nm fibre level (well below light microscope resolution) is often found in "unambiguous" breaks (Brecher, 1977). One may ask why the distinction is important. One reason is that much of the theory of aberration formation turns upon the frequency of true "breaks". Another is that breaks lead to genetic loss and cell death whereas gaps do not appear to be genetically important, nor do they appear to give rise to subsequent aberrations.

Which leaves us with the question "What then are

gaps?" Whilst a spectrum of damage underlies the phenomenon, it is very likely that the gaps themselves represent errors or failure in chromosome condensation and packing, and so constitute a rather different event from that which leads to structural change. It is important therefore that they be excluded from theoretical analysis of aberration formation.

Isochromatid breaks (pp. 202–205)

Because of its importance in his later theoretical discussions and calculations, Lea singles out this class for special consideration. It is, however, only one member of a group of four possible intra-arm intrachanges. The other members, whilst not visually so obvious, can, with care, be recognized and scored (see below, Fig. 1).

All four members are readily derivable from a "Revell loop" (Revell, 1959; Savage, 1986) and their relative frequencies form the basis for numerical tests of the "exchange hypothesis", which was to challenge the "breakage and reunion" ideas fundamental to Lea's theories (Revell, 1974). We will return to this point later.

Lea states (p. 202) "both chromatids are broken at the same level ... believed to be produced by a single ionizing particle which passes through and breaks both of the chromatids of the already split chromosome". He correctly recognizes them as chromatid-type changes, but careful studies indicate that the sister chromatids are not necessarily (perhaps never) broken at the same locus and there is now evidence for a two-track component in their formation. Indeed, the use of a quadratic to fit a dose-response curve was first introduced by Lea and Catcheside (1942) to take account of curvature in the data for isochromatid breaks in *Tradescantia*.

The argument Lea invokes (p. 202) for their post-split nature, namely that they are contemporary with chromatid interchanges, is not conclusive as it stands since, as was pointed out above, split and unsplit regions exist together throughout S. But as we can now identify unambiguously post-S cells, and in these we find isochromatid aberrations, the matter seems settled.

The evidence cited (p. 202) for their one-track origin [that ultraviolet (UV) radiation does not induce them] is invalid. Later work showed that UV can produce *all* types of chromatid change in *Tradescantia* pollen tubes with high efficiency (Kirby-Smith & Craig, 1957) and this has been confirmed in mammalian cells (Bender et al, 1973). In passing, the efficiency of UV in the pollen tube system is, in itself, very remarkable. Unlike ionizing radiation, it is usually necessary for the cell to pass through a normal ("scheduled") DNA replication cycle to convert UV lesions to aberrations (Bender et al, 1973). Thus aberrations are not readily formed in G₂ cells. Yet, the generative cell of the pollen grain is in G₂, for DNA synthesis takes place some 2–3 days before the pollen is used for experiments!

When gaps are excluded, the isochromatid/chromatid ratio does not change as dramatically as Table 49 (p. 203) indicates, and if S-phase cells are also excluded, the change within G₂ appears to be negligible. [Note

that these early workers used "prophase" to cover what is today regarded as prophase, G_2 and most of S-phase (Savage, 1975)].

The various forms of end-union (SU, NUp, NUD, p. 204 and see Fig. 1) do vary in relative frequency through the cycle and also to some extent between different organisms. NUpd, which cannot (except in post-S cells) be distinguished from a chromosome-type terminal deletion, appears to be very rare in plants, but more frequent in animal cells.

High-linear-energy-transfer (LET) radiations like α particles do produce more unrejoined breaks (p. 204) but this may not be due entirely to the existence of more heavily damaged, unrejoinable, broken ends. These radiations produce a higher frequency of complex, multibreak intrachanges (Savage, 1976), many of which simulate simple intrachanges, but have less opportunity for full rejoining. A similar phenomenon is found with chemically produced aberrations.

Footnote 1 (p. 205) draws attention to a very important point that has frequently been overlooked in radiation cytogenetics, namely that because of mitotic delay and perturbation, time of observation after treatment is *not* equivalent to time before metaphase (*i.e.* the position of the cell in the cycle when treated). This is just a facet of the much wider problem of "imprecision" present in any asynchronous cell population, perturbed or unperturbed. Put simply, because cells move through the cycle at different rates, two cells observed together at metaphase have never before been together at the same stage of the cell cycle. The further you move back in the cycle (or the later you sample after treatment) the greater the divergence between the stages represented. This means that random samples of metaphases, sequentially sampled after radiation, come from an ever increasing range of cell stages. Consequently, quantitative precision falls, and this has a profound effect on such problems as relating aberration yields to cell stage sensitivity and to obtaining reliable quantitative measures of damage. Synchronous cell populations are *not* free from such problems. For fuller discussions see Savage and Papworth (1973a, 1975).

Chromosome intrachanges (pp. 205-207)

With conventional staining, only the *A* forms (centric ring, interstitial deletions) can be scored with accuracy. The introduction of chromosome banding in mammalian cells (Seabright, 1971; Sumner et al, 1971) allows most of the centric *S* forms (pericentric inversions) to be scored but only a small proportion of the paracentric ones, and that with variable efficiency between chromosomes (Savage, 1977b).

The anaphase separation patterns Lea describes ("fall free", "dicentric ring", "interlock") are readily derived from twists in the cleavage plane of a Möbius band. However, they could equally well be derived from sister-chromatid exchanges within the ring, occurring at the time of replication. In general, the complexity of the configuration is a function of loop size, and smaller

rings invariably "fall free". Acentric rings and interstitial deletions always adhere in the absence of spindle fibres to separate them.

The bridge breakage and fusion cycles are well established and account for the very variable size of persistent centric rings found clinically (Kistenmacher & Punnett, 1970).

On p. 206 Lea raises a question that applies to all aberrations, "whether the alternatives (*i.e.* *A* and *S*) are equally probable". Because only *A* chromosome types can be scored with accuracy, he resorts to indirect inference from the highly selected situation in *Drosophila*. The advent of chromosome banding has given us the first direct evidence that *A* and *S* are truly alternative modes (Savage & Papworth, 1982).

The frequency (absolute and relative) and size range of interstitial deletions ("minutes" and "isodiametric fragments") show considerable variation between organisms. The peaked size curves are probably an artefact of microscopical resolution for it is established that they can occur down to the molecular level (Thacker & Cox, 1983).

Chromatid intrachanges (p. 207)

Lea confines discussion to the centric (interarm) intrachanges of which there are four types, all with different genetic consequences but which can only be resolved as two types at metaphase (Savage, 1976).

As mentioned earlier, there are also four types of intra-arm intrachanges (Fig. 1) but he only deals with one under a separate section (isochromatid breaks, p. 202). Historically, this particular group has assumed very considerable importance. From detailed studies of both chemical and radiation-induced intrachanges, Revell advanced his exchange hypothesis that was to become the first major challenge to the Lea/Sax "breakage followed by reunion" (Revell, 1959, 1974; Evans, 1962; Savage, 1976, 1986).

Very briefly, Revell argued thus: The four intra-arm intrachange types would produce eight singly incomplete forms (Fig. 1). Two of these (4a, 4b) would be seen as NUp and NUD isochromatid breaks and five (1a, 1b, 2a, 3a, 3b), without very careful examination, would look just like simple terminal deletions. The remaining one (2b) would be most likely scored as a minute. Revell suggested that *all* aberrations arise from an exchange process and that *all* observed "breaks" were *secondary*, resulting from failed exchanges and not *primary* as the classical theories believed. Certain numerical predictions followed from these ideas, and once the "gap" *versus* "break" distinction was made, the early tests confirmed the predictions. Clearly, this was a most fundamental undermining of established ideas upon which everyone was building, and the bitter furore that raged led to numerous experiments to "prove" or "disprove" the new theory. These experiments have done little to settle the controversy but they have served to show that the process of aberration formation is very much more complex than either camp had foreseen!

Today, we recognize that many "breaks" are indeed

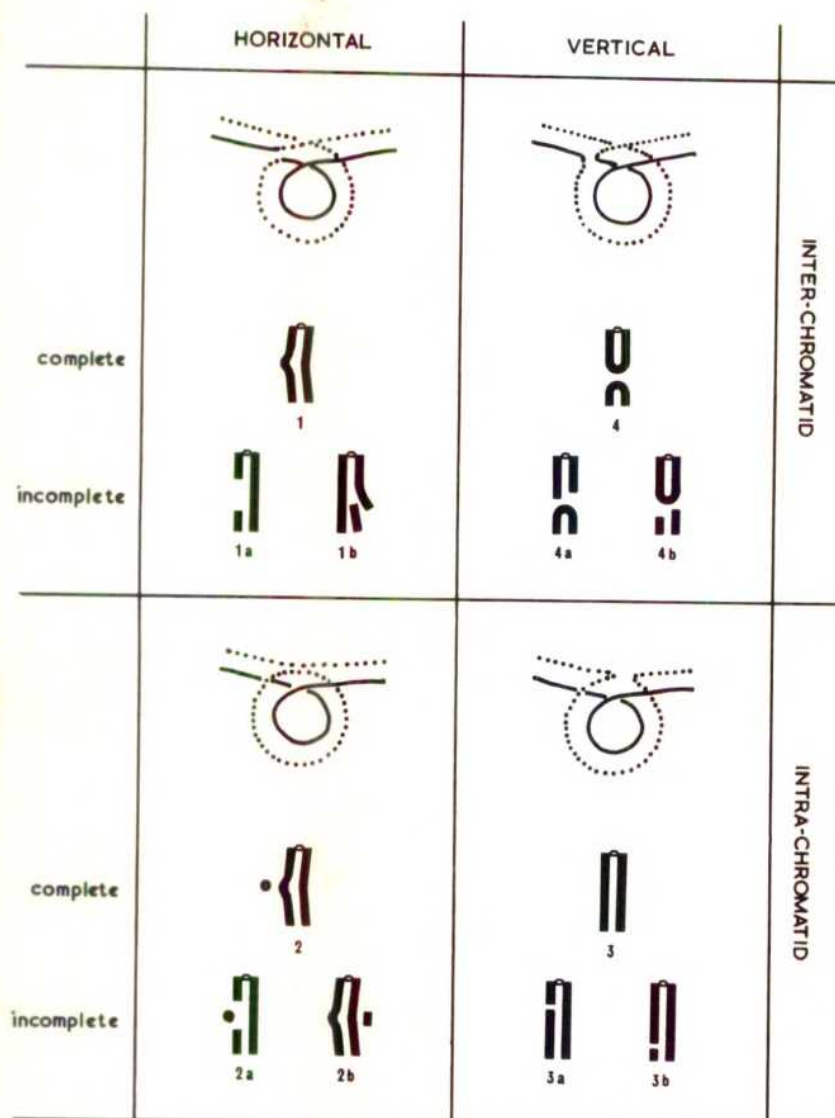


Figure 1. The simple (one-event) chromatid intra-arm intrachanges and their derivation from a "Revell loop". In the loop, sister chromatids are distinguished by solid and dotted lines. Horizontal/vertical refers to the orientation of the exchange with respect to the arrangement of chromatids in the "neck" of the loop. There are four possible complete and eight singly incomplete forms. [From Savage (1986), with permission of the Association of Clinical Cytogenetics.]

failed intrachanges but that true "primary" breaks do exist, and at the molecular level the double-strand DNA break is a very strong candidate for the origin of many aberrations (Kihlman 1971; Bender et al, 1974a; Chadwick & Leenhouts, 1981). Qualitatively identical aberrations can be produced by a very wide variety of agents. Some of these introduce specific lesions into the DNA that are not breaks and the aberrations arise via various repair mechanisms (misrepair?). It is doubtful therefore whether we should think any longer in terms of a single mode of formation, even for radiation.

In retrospect, many of the numerical tests of the exchange theory were doomed to failure, for they presuppose that all intrachanges are simple, two-lesion events. It is now clear that many that look simple are, in reality, multilesion events (Savage, 1976), which

simulate simpler forms but have quite different incompleteness characteristics. Moreover, incompleteness is not constant through the cell cycle so that heterogeneity in samples modifies observed relative frequencies.

Interchanges (pp. 207–211)

These are the most obvious and least ambiguous aberrations, and hence of considerable value for reliable numerical analysis. "Chromosome dicentrics" in human cells today form the backbone of "biological dosimetry", as used in radiation protection and nuclear accidents (Ishihara & Sasaki, 1983; Lloyd, 1984).

For chromosome types, only the *A* form (dicentric) is regularly scorable. The *S* form ("reciprocal translocation") requires chromosome banding for

detection on a regular basis. This latter form is transmissible and so assumes importance in clinical and cancer studies.

In contrast, because of sister-chromatid adhesion, both *A* and *S* chromatid-type interchanges can be scored with equal facility.

The segregation patterns at anaphase (p. 208) and the rates of loss of *A* forms have been extensively studied. There are significant differences between organisms. Dicentrics can persist for many years after radiation in humans (Savage & Bigger, 1978; Buckton, 1983) and are still found in Japanese atomic bomb survivors (Awa, 1983).

The relative frequency of *A:S* (pp. 209–210) has proved another area of controversy. As indicated above, evidence for chromosome types suggests equal likelihood. For chromatid interchanges, however, there is a strong indication in some organisms that $A > S$ (Evans, 1962) but not in *Tradescantia* (Savage, 1975). The issue is clouded by sampling problems, for there is some evidence that *A:S* may change through the cycle (Brewen et al, 1969). There are also additional complicating torsional and polarity problems that affect chromatid exchanges and these will influence final observed ratios (Evans, 1962; Wigglesworth & Savage, 1977).

The apparent equality of *A:S* prompted the suggestion (p. 210) "that there is no evidence ... of any polarization in the chromosome such as would prevent random joining of broken ends ... this fact makes it improbable that breakage and union occur in linkages in a polypeptide chain, since such linkages are polarized". What Lea of course did not know was that DNA is a twin-stranded molecule, each strand polarized in the opposite direction. Rejoining is permitted only within these polarity constraints and this has been amply demonstrated by following the chromatin segregation patterns in subsequent cell generations (e.g. Olivieri et al, 1973; Bender et al, 1974b).

Relative frequency of interchanges and intrachanges (pp. 211–214)

The calculations used (p. 212) to obtain the expected ratio of intra-arm intrachanges to inter-arm intrachanges to interchanges are based on four presuppositions:

1. Complete independency of the three aberration categories.
2. Equal likelihood of all categories.
3. Complete random participation amongst arms.
4. All arms in the karyotype are of equal length.

Presupposition 1 is probably true, but there is little hard experimental evidence either way. The remaining assumptions are all invalid although 4 is approximated in *Tradescantia*. The discrepancies are not, therefore, surprising and would have been much larger had the full data been included (p. 213).

Calculations like this fail to take into account factors such as the spatial limitations within the interphase nucleus. In all organisms investigated, the ratio of

dicentrics to centric rings is always significantly lower than expected [in *Tradescantia* assuming 12 equal arms we expect 10:1 and observe ~3:1 (Sax, 1940; Savage, 1970; Savage & Papworth, 1973b)]. Intra-arm intrachanges are also very frequent, and would be even more so if there were not limits on microscopical resolution.

If such probability differences are taken into account, then consistent relative relationships can be found amongst chromosome-type aberrations (Chadwick & Leenhouts, 1981). However, when computing such parameters as the participation of arms in exchange (see next section) these different relative probabilities require the various aberration categories to be separated—they cannot be included within the same contingency table. The lumping together of "breaks" irrespective of origin (alas, a frequent mistake) only leads to confusion.

For chromatid-type changes, relative as well as absolute frequencies of different categories change as the cell transits the cycle, so that simple inter-relationships do not exist.

Locations of breaks in chromosomes (pp. 214–216)

This is a difficult area, and one which has received new impetus in recent years with the arrival of chromosome banding techniques and with the realization that specific recurrent visible chromosome changes are associated with certain cancers and some genetic diseases.

Experimental literature is often confused, because several factors, which are not necessarily related, are often confused—the *allocation* of breaks to arms, the *distribution* of breaks within arms, and the *participation* of arms in exchange aberrations (Savage & Papworth, 1982). Additionally there are the difficulties of obtaining a truly random unbiased sample of breaks, of segregating aberration types, and perhaps the most difficult problem of all, the "length at risk" to be used in any statistical tests for randomness.

Lea touches only on three facets of the topic (eu- versus heterochromatin, break location and relation to arm length). He concludes (p. 215) that euchromatic and heterochromatic chromosome regions are approximately equally breakable. Two types of heterochromatin are now distinguished: "constitutive", that which is a permanent feature of the chromosome (or at least the chromosome in cultured cells), and "facultative", that which can become heterochromatic in certain cells or at certain stages of development (e.g. one X chromosome in female XX cells). Heterochromatin is characterized by its late time of replication (Brown, 1966). For radiation, there is very little evidence that either type of chromatin is more breakable but there is a definite bias towards late-replicating chromatin for chemically induced aberrations (Brogger, 1977), although in some cases this may be an artefact of cell selection.

We have had occasion several times to refer to the new techniques of chromosome banding. These produce alternating segments of dark and light chromatin along the chromosome when Giemsa stain is used, the pattern

being a fixed and specific characteristic of the chromosome region that can be used for identification. The bands are similar to, but not as detailed as, those of the *Drosophila* polytene chromosomes to which Lea refers.

In addition to chromosome identification and the observation of otherwise invisible symmetrical chromosome-type changes, the alternating pattern offers a more objective method for locating "break points". The most commonly used techniques result in a "G-band" pattern (ISCN, 1978, 1985) and break points tend to be predominantly in the pale-band regions. For chromosome-type changes, this could be the result of a pattern-recognition artefact (Savage, 1977a,b) but since it occurs with chromatid-type aberrations also, it may represent a real bias.

Lea raises the question "whether certain points are specially liable to be broken" (p. 214) and the second edition appendix note (p. 366) cites affirmative *Drosophila* evidence. We now term such regions "hot-spots" (and recognize that there may be reciprocal "cold-spots"). The answer is "yes", although experimentally many claimed hot-spots are very variable in expression, which may reflect sampling problems.

Recently it has been shown that certain specific regions are, in some individuals, prone to spontaneous and induced breakage. These have been termed "fragile-sites" and at least one of them (fra Xq 27) is clearly associated with a form of mental retardation (Sutherland, 1983) and there are claims that others are identical with sites commonly broken in some forms of cancer (Yunis et al, 1987).

In all tests for randomness, some concept of chromosome length or "length at risk" is needed. New understanding of the complexities of intranuclear architecture, of localized chromosome domains, of the association of chromatin with the nuclear membrane, and of the dynamic changes in chromosome condensation during progress to mitosis make it seem unlikely that a simple static parameter like "mitotic length" (p. 215) is a really valid basis for such tests.

Frequency relations (pp. 217–220)

On the assumption of a random allocation of breaks and their free participation in aberrations, the form of the distribution of aberrations between cells will be "according to the Poisson formula" (p. 217).

Such tests presuppose a random, unbiased sample of the original target cells. Any element of non-random cell selection is guaranteed to warp the distribution, as is seen in the anomalies of Lea's *Drosophila* data.

The χ^2 test is rather insensitive for distribution studies because of the requirement to lump the tail data. Better tests are available (Savage, 1970) and powerful computers allow "exact" tests (Papworth, 1983). When these more sensitive tests are used many aberration distributions show "over-dispersion", which is almost certainly an indication that the sampled (and probably the target) population is heterogeneous with respect to radiosensitivity (Couzin & Papworth, 1979).

Interestingly, the significant departures in Lea's Table 56 (p. 218) are all in the direction of under-dispersion, a condition unlikely to arise from heterogeneity. Underdispersion turned out to be a regular feature of dicentrics and rings in *Tradescantia* and this observation coupled with the frequently observed $\frac{3}{2}$ power of the dose-response curve for exchanges (p. 212) led Wolff and his colleagues (Wolff, 1963; Atwood, 1963) to propose that there were only a limited number of sites within the nucleus where exchange could take place. The necessary corollary of site limitation—a saturating dose-response curve—was soon demonstrated and another lively controversy was precipitated. From this an alternative hypothesis emerged based on the fact that although a chromosome arm may participate in more than one exchange it can never be *seen* to be involved in more than one. Thus there is a progressive "loss" of exchanges as the dose increases. Obviously cells with fewer chromosome arms will be the most affected and this was found to be the case (Savage, 1970). It follows that the observed dose-response curves in low chromosome numbered organisms like *Tradescantia* are "distorted" or warped and need to be corrected for the lost exchanges *before* mathematical curve fitting (Savage, 1969). Distortion does not apply to intra-arm intrachanges or terminal deletions, nor to any type of chromatid aberration, which again alerts to the danger of pooling "breaks" for tests or for predicting combinatorial distributions (second edition Appendix II, p. 366).

Modifying factors (pp. 220–225)

As we approach this section, we have to recall that the prevailing philosophy when Lea was writing was competition between restitution and rejoining amongst a collection of flapping broken chromosome ends. Increases or decreases in aberration frequency, resulting from some treatment additional to radiation, were interpreted as favouring or promoting one or other of the joining modes. The importance of metabolically mediated repair mechanisms and of the physiological state of the cell were not then fully appreciated.

Towards the end of this section (p. 225), Lea touches on the problems arising from variations in radiosensitivity as the cell transits its cycle towards metaphase and the difficulties of ascertaining where cells were in cycle at the time of treatment because of mitotic perturbation introduced by radiation.

It is surprising, therefore, that he (and many others since) did not recognize that these modifying treatments are, in many cases, either exacerbating or revealing this heterogeneity, without necessarily affecting the fundamental aberration-forming mechanisms.

For example, at growth temperatures of $\sim 20^\circ\text{C}$, chromatid-type aberration frequencies in *Tradescantia* microspores rise to a distinct peak ~ 16 h post-irradiation. The height and position of this peak are markedly influenced by radiation dose, temperature, infrared light and mechanical stress, yet a single sample time of ~ 24 h was used for all treatments by all

experimenters. Thus, different parts of the peak and different cell mixtures would be sampled, so fluctuations in yield are difficult to interpret. A classic example of this trap is the infrared aberration yield modification, which after much work and interpretation was shown to be simply due to single sampling of delayed populations (Ma & Wolff, 1965). Similar criticisms may be made of the cited work for colchicine (p. 220), ultraviolet (second edition, Appendix II, p. 368) and ammonia (p. 223), with the added point that these treatments are to some extent cell-lethal so that a limited and selected population of cells arrives at metaphase for scoring.

Leaving aside the multitude of chemicals that themselves produce aberrations, there are many that genuinely modify aberration frequency if given at the right time in relation to the radiation. A good example is caffeine (Kihlman, 1977) and there are a number of radiosensitizing compounds that have become important in radiotherapy (Stratford et al, 1983).

Mechanical stresses like centrifugation (p. 220) have profound effects on cellular physiology and hence on energy-dependent repair processes (Evans, 1962). It was not long therefore before the seemingly clear-cut results reported here became very confused (Wolff & von Borstel, 1954; Yeagers, 1964).

Since Lea's day, many modifying factors have been added, probably the most important of which is oxygen (Thoday & Read, 1947). This substance plays a role at two levels:

1. Its presence or absence at the time of radiation determines the degree of initial damage, the magnitude of the effect depending on the LET of the radiation. For X or γ rays the oxygen enhancement ratio (OER) for aberrations is 2.5–3.
2. Most of the repair/rejoining mechanisms as well as normal cellular processes are dependent on energy derived from oxidative metabolism and prolonged anoxia plays havoc with cell physiology.

For a fuller discussion of the oxygen effect see Alper (1979).

A surprising number of aberration yield modifications have ultimately turned out to be oxygen effects. Almost certainly some of the increased frequencies with irradiation at low temperature (p. 222) arise from increased oxygen solubility and reduced metabolism.

A demonstrable oxygen gradient is present in anthers of plants growing in air, which adds to cellular heterogeneity (Beatty et al, 1962), and this needs to be taken into account in, for example, dose-response curve work (Savage, 1965).

On p. 224–225 Lea discusses stage sensitivity and points out that “the highest sensitivity is reached in prophase” ($\equiv G_2$ in modern terms). This raises the question of whether post-split chromosomes are *intrinsically* more sensitive than pre-split ones. This has never been answered satisfactorily, partly because of the difficulty of getting a unique frequency for chromatid aberrations and partly because one can score so many

more types of change in split chromatids, some of which are invisible or impossible in unsplit ones.

As Lea states, irradiation of late prophase-metaphase only produces aberrations in subsequent cell generations.

Dependence of the yield of structural changes on radiation intensity (pp. 225–229)

This section also touches on dose fractionation (p. 226). In general, the effects reported have been fully substantiated in a wide variety of materials. For low-LET but not high-LET radiations, the observed frequency of exchange aberrations falls to a lower level as the exposure time (the time taken to deliver a given dose) is increased or the time interval between fractions given at constant dose-rate is increased. Only aberrations involving the interaction of two or more breaks are affected.

The given explanation is that because breaks have a finite lifetime in which to rejoin, “a break in one chromosome has time to reconstitute before another break is produced in its vicinity with which exchange is possible” (p. 226). The absence of effect with high-LET radiations results from the fact that both requisite breaks are produced by the passage of one ionizing track.

Not surprisingly, further experimentation has indicated that these explanations are only part of the story. The magnitude and rate of fall as exposure time is increased is markedly dose-dependent, suggesting that even for low-LET radiations a proportion of exchange events arise from the passage of one ionizing track (Purrott & Reeder, 1976b).

In the case of fractionation, the time taken to reach the “baseline” (the yield expected if the fractions are simply additive) is also dose-dependent, and the observed yield frequently falls *below* the baseline or sometimes fails to reach it (Purrott & Reeder, 1976a). From time to time, people report “Lane effects” (Lane, 1951; Evans, 1967; Sasaki, 1978), where the falling yield suddenly shows a transitory rise as the fractionation interval continues to increase. These phenomena may be indications of cryptic heterogeneity in the target population.

All explanations presuppose, and indeed require, that the target cell population is homogeneous in its sensitivity. Unfortunately this has rarely been the case and many fractionation experiments remain suspect on this ground. Thus much of the work done with dormant *Vicia* seeds to characterize the rejoining parameters and energy requirements needs re-examination because it has been shown that, in spite of the uniform resting (G_0) cell population, the heterogeneity of sensitivity leads to significant aberration fluctuations with sampling time (Miller & Colaiace, 1970). A similar criticism must be made of the chromatid aberration fractionation work.

Dependence of yield on dose (pp. 229–237)

The form and quantitative analysis of dose-response curves continue to play a major role in radiobiological theory, “the main basis on which theories of the

mechanism of induction of these (chromosome aberrations) are built" (p. 229).

The main findings reported have been abundantly confirmed in subsequent work:

1. With low-LET radiations, exchange aberrations increase curvilinearly with increasing dose whilst simple "breaks" increase approximately linearly. A few authors have reported curvature for terminal deletions [Brewen and Brock (1968) in wallaby lymphocytes] but the possibility of second-division contamination of the scoring sample cannot be ruled out. There is also the problem, mentioned earlier, of making an absolute distinction between terminal and interstitial deletions, the latter having a distinctly curving dose-response (Rick, 1940).
2. With high-LET radiations, all classes of aberrations increase linearly with dose.
3. If the dose-rate is lowered and kept constant (variable exposure time), the degree of curvature falls with low-LET radiations until it approaches linearity at very low dose-rates.
4. If the exposure time is kept constant (variable dose-rate) the curvature is usually more obvious, but very little experimentation has been done in this mode since the Lea-Sax era.

These observations were readily interpretable in terms of the interaction of breaks with finite lifetimes. For low-LET radiations the majority of these breaks are produced by the passage of a single ionizing particle whereas the majority of interacting *break-pairs* are produced by a single particle for high-LET radiations.

Lea and his colleagues introduced the use of a quadratic to fit the slight curvature observed in the dose-response curve for isochromatid aberrations (Lea & Catcheside, 1942) and later expanded this to interpret the linear and quadratic coefficients in terms of "one hit" and "two hit" events (see second edition, Appendix II, p. 370). Following this tradition, a multitude of biophysical models has been produced to take account of time-intensity factors, target size, site number, track structure, repair, etc. (Neary, 1965; Kellerer & Rossi, 1972; Savage, 1975; Goodhead, 1980, 1983, 1987; Chadwick & Leenhouts, 1981; Harder, 1987). Many of these models have a multiplicity of terms and can therefore fit almost any set of data. Whether the derived parameters can be equated directly with biological or biophysical events is debatable.

No amount of sophisticated mathematical analysis is of any avail if the initial dose-response curve is warped or distorted. Lea draws attention (p. 232) to one form of distortion that results from the time-intensity phenomenon, and later attempts a mathematical solution (the famous G-function, p. 262-269, Appendix II, p. 373). Mention has been made earlier of another form of distortion, present in *Tradescantia* and other low-chromosome-number cells, arising from the inability to observe more than one dicentric per chromosome arm (Savage, 1970). Correction for this must be made before the response curve is analysed

(Savage, 1969). In the absence of correction, a pure "square-law curve" cannot be obtained, even though one might be theoretically expected (p. 232).

Finally, there is the frequent use of cell systems that lack homogeneous radiosensitivity so that the observed aberration frequency changes with sample time. Obviously, in the absence of a unique yield to set against a specific dose, no meaningful response curve can be produced (Savage, 1978). Such is the case for all known chromatid-type ("post-split") aberration systems. The profiles of all response curves produced from these cannot therefore be used in biophysical modelling. This is a serious weakness that underlies some of the arguments advanced by Lea in the later chapters of his book. Fortunately, the "pre-split" chromosome-type system in *Tradescantia* [and the resting *human* blood lymphocytes, now widely used (Scott & Lyons, 1979)] can, with appropriate precautions, be taken as homogeneous with respect to radiosensitivity. This is *not* automatically true for all "pre-split" cell populations, an assumption that is often erroneously made (Miller & Colaiace, 1970).

On p. 235 the use of scoring "abnormal anaphases" (*i.e.* anaphases showing bridges and/or fragments from aberration segregation) is discussed. Data are usually presented as log per cent "normal" anaphases plotted against linear dose (Fig. 36, p. 236), in familiar "survival curve" manner (Alper, 1979). Lea recognized the limitations compared with full metaphase scoring, but points out the convenience. Interestingly, he draws attention (p. 235) to the frequent absence of curvature when it might be expected from the known dose-response curve of the originating damage, and unknowingly indicates another much more serious limitation of this method. It turns out that there is a progressive loss of bridges (and probably fragments also) as the dose increases (more specifically as the metaphase aberration frequency increases) so there is a concomitant loss of upward curvature, to give saturation and a peak at high doses.

This means that the efficiency for detecting damage is dose-dependent and therefore the method is not to be recommended (Wolff & Luppold, 1957; Conger & Curtis, 1966). The reason for this bridge "loss" is still unknown.

The relative efficiencies of different wavelengths and types of ionizing radiation (pp. 237-240)

"Study of the relative efficiency of radiations of different ion density in producing structural changes in chromosomes is an important method of attack on the mechanism of this process" (p. 237), and so it has proved. We now know so much more about the nature of the target, the modes of energy deposition, and of track structure and there are many more qualities of radiation available for investigation.

For structural aberrations, the reference radiation is usually X rays of ~200 kV, and the absorbed dose of this radiation to produce a specified frequency is divided by the absorbed dose of the radiation in question producing the same yield under identical conditions to

give the relative biological effectiveness (RBE) [International Commission on Radiological Protection (ICRP), 1963].

When the RBE is plotted against some measure of energy deposition (*i.e.* LET) a humped curve results, with the peak in the region of $100 \text{ keV } \mu\text{m}^{-1}$ (Alper, 1979; Chadwick & Leenhouts, 1981).

In many cases, as Lea points out (p. 238), a unique value for RBE cannot be given because there are differences in the shapes of the dose-response curves. Higher values are found at lower doses, which is of course important in the context of radiation protection. In such cases, the concept of a "limiting value" has been used, for at very low doses all response curves tend to linearity. When quadratic analyses of the response curves are made, the ratio of the linear coefficients is often used to approximate this limiting value, on the assumption that this coefficient represents that portion of the damage unaffected by dose-rate.

The discrepancies for α particles alluded to on p. 239 arise primarily from the use of chromatid-type aberrations, coupled with the enormous kinetic perturbations and interphase death produced in the heterogeneous cell populations by these very high-LET particles.

Even in homogeneous populations anomalous exchange formation and distributions arise because of the highly localized energy depositions confined to a few discrete tracks (Edwards et al, 1980).

Perhaps the most important and fundamental change that has affected Lea's concepts is the finding that, contrary to the statement of p. 240, ultrasoft X rays (even down to the characteristic carbon K which generates electron tracks with extended range $< 7 \text{ nm}$) are highly efficient in producing aberrations, mutation and cell killing (Neary et al, 1964; Goodhead, 1983). This indicates clearly that the target size and rejoining distance for aberrations are much smaller than Lea envisaged, and run counter to the predictions of many biophysical models based on sub-lesion interaction over long distances. Rather, the results suggest that damage arises predominantly from occasional concentrations of energy in very small volumes of nanometre dimensions. Such localized concentrations of energy will be found also in the track ends of longer path electrons generated by hard X rays, which is in line with ideas put forward by Lea (pp. 273-277).

The reasons for the major experimental discrepancy between Lea's and Neary's findings probably lies in the *Tradescantia* pollen-tube system. It does not take much damage to render the generative cell's metaphase unscorable, even unrecognizable. Thus scoring is biased in favour of "normal" cells, a bias that increases with dose. It was the use of very low soft X-ray doses that led to Neary's discovery of their efficiency (Neary et al, 1964).

Coefficients of aberration production in *Tradescantia* (pp. 240-241)

The values given here are now only of historical

interest, and for reasons given above those for chromatid-type aberrations must be taken with extreme caution. The derivation of coefficients is a mathematical exercise (Savage, 1975), their validity dependent upon an unwarped dose-response curve, and their usefulness a function of the interpretation given to them.

Structural changes induced by ultraviolet light (pp. 242-244)

Ultraviolet-light-induced aberrations fall outside the remit of this review, and since Lea's day have become the topic of great interest [World Health Organization (WHO), 1979]. Suffice it to say that we now know that the *whole* range of chromatid-type aberrations can be produced (but not primary chromosome type), that the lesions are *not* breaks in Lea's sense but principally pyrimidine dimers within the DNA molecule, that the aberrations are produced as the result of several very specific and efficient repair mechanisms already present in the cell (Scott, 1980; Kimball, 1987), and that in mammalian cells, the chromosomes must pass through a scheduled DNA synthesis phase to convert the lesions to aberrations. Most of these facts are in marked contrast to aberrations production by ionizing radiation but very similar to the production of aberrations by many chemical agents. It therefore would seem to be unwise to use UV findings to back up theories for the action of radiations. Useful discussions of similarities and differences will be found in Kihlman (1971) and Bender et al (1973, 1974a).

Conclusion

As was to be expected, time has shown that the mechanism of aberration formation is very much more complicated than was at first thought. An enormous variety of substances and treatments are now known that can produce qualitatively identical structural changes in chromosomes to those found with irradiation. This cautions us against expecting one unifying process for their induction. It also suggests that chromosome aberrations may be a rather non-specific end-point and in this connection it is important to remember that there is a strictly limited number of ways in which chromosomes can be "broken" and "rejoined" to give different configurations.

The irradiated cell has available a battery of inbuilt repair systems (some, perhaps, inducible) to deal with any DNA damage sustained. We observe, therefore, not so much the cell's reaction to that damage, but rather its inability to cope with some qualitative and/or quantitative aspect of it, *i.e.* our results probably tell us more about the cell than they do about the treatment. It is not surprising, therefore, that current research interest in the field of aberrations is focusing on specific molecular lesions and how the cell handles them, what repair pathways are available and what proteins and genes are involved in them. The continued development of powerful molecular-biology techniques is greatly aiding such studies and is carrying our resolution down to the site of the primary radiation events. I am sure had

Douglas Lea lived, he would have found these developments very exciting.

In his preface to the second edition (1955), L. H. Gray said of Lea's book, "I believe it is of permanent value to the student of radiobiology, however far our knowledge of the phenomena treated by Lea may transcend that which was available to him". The brief update that I have attempted in this review confirms this and shows what a very solid foundation Lea laid for us to build on.

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Orbital intraconal haematic cysts in young people: computed tomography and magnetic resonance imaging

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Abstract. Eight cases of focal non-traumatic haemorrhage into the intraconal retrobulbar space in children or young adults have been examined by computed tomography. The lesion is seen as a smoothly rounded, localized mass, which does not extend to fill the intraconal space. Magnetic resonance imaging in two cases did not reveal the expected high signal on T_1 -weighted images, but in most patients the combination of clinical and radiological features is sufficiently indicative of the diagnosis to allow conservative management.

Non-traumatic, intraorbital haemorrhage typically presents as acute, often severe, orbital pain, with a variable degree of proptosis. Venous anomalies underlie many cases (Krohler & Wright, 1979). In older patients, the blood rapidly tracks forwards to the conjunctiva making the diagnosis obvious, but, in children especially, the blood may remain localized and become encysted, forming a discrete, intraorbital mass lesion, a "haematic cyst". This often occurs when the blood is subperiosteal, but the present report concerns eight patients with haematic cysts within the muscle cone.

Material and methods

Eight patients underwent full clinical assessment in the Orbital Clinic at Moorfields Eye Hospital. All were examined by X-ray computed tomography (CT) and two also underwent magnetic resonance imaging (MRI) using T_1 -weighted inversion-recovery (IR) and T_2 -weighted spin-echo (SE) sequences at the National Hospital, Queen Square. Surgical confirmation of the

nature of the orbital lesion was obtained in all but two patients (see below).

Results

The clinical features are summarized in Table I. Brief case histories of the seven patients, including findings on imaging, follow.



Figure 1. Case 1. Unenhanced axial CT scan showing a well defined, rounded mass of soft-tissue density (arrow) lying between the left optic nerve and the lateral rectus muscle.

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Table I. Summary of clinical features

Case no.	Sex/age	Aetiology	Time from bleed to imaging	Visual impairment	Pain	Proptosis	Surgery	Multiple episodes
1	F/13	Spontaneous	2 weeks	No	No	Yes	Yes	No
2	F/10	Spontaneous	3 weeks	Yes	Yes	Yes	Yes	Yes
3	F/12	Spontaneous	3 weeks	Yes	No	Yes	Yes	No
4	M/14	Spontaneous	4 days	No	Yes	Yes	Yes	No
5	M/24	Spontaneous	6 months	Yes	Yes	Yes	Yes	No
6	M/14	Spontaneous	3 days	Yes	Yes	Yes	No	Yes
7	F/26	Spontaneous	1 day	Yes	Yes	Yes	No	No
8	F/15	Previous optic nerve glioma	3 months	N/A	No	Yes	Yes	Yes

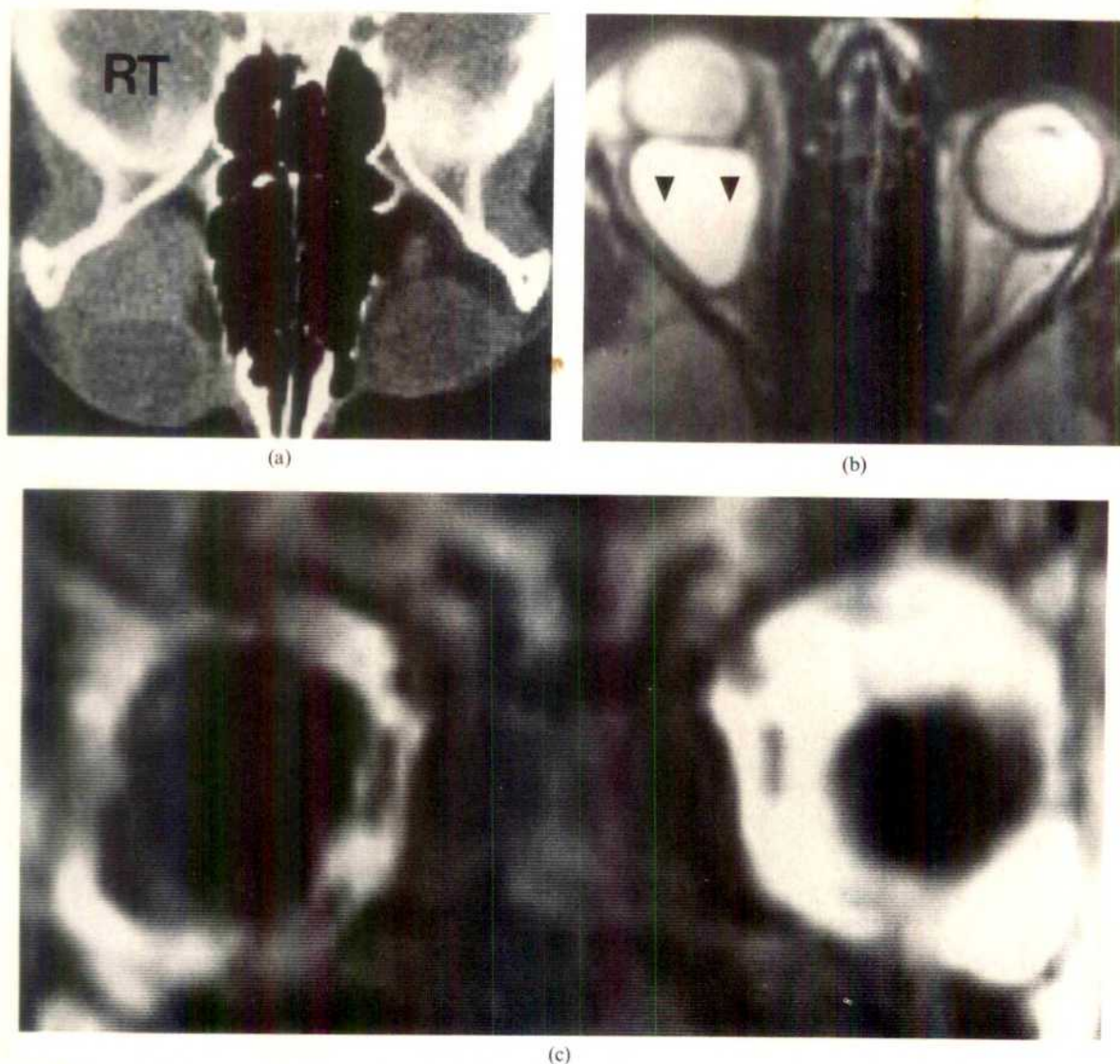


Figure 2. Case 3. (a) Unenhanced CT scan (patient prone). A rounded mass, slightly denser than brain, fills the intraconal space. (b) MRI (SE 2000/80) in supine position shows a fluid level (arrowheads) within the mass, whose otherwise uniform high intensity also indicates its cystic nature. (c) Coronal inversion-recovery (1500/500/40) image suggests more internal texture, but shows predominantly low signal within the lesion.

Case histories

Case 1. A 13-year-old girl presented with a 2-week history of painless left proptosis; vision was unaffected. Computed tomography demonstrated a discrete, rounded, intraconal mass lesion (Fig. 1). At surgery, an encysted blood clot was encountered, histological examination of whose wall showed no evidence of an underlying lesion. Recovery was uneventful.

Case 2. A 10-year-old girl presented with a 3-week history of painful left proptosis of acute onset; visual acuity on the affected side was reduced to 6/12.

Computed tomography revealed a rounded, intraconal mass. The cyst was drained on two occasions, and histological examination was compatible with simple haemorrhage. Recovery was complete.

Case 3. A 12-year-old girl gave a history of 3 weeks painless right proptosis. Visual acuity on the right was 6/60. Computed tomography showed simply a rounded, homogeneous mass lesion filling most of the intraconal space, but axial T_2 -weighted spin-echo (SE 2000/80) MRI showed a lesion giving high signal, with a fluid level between two homogeneous components (Fig. 2).

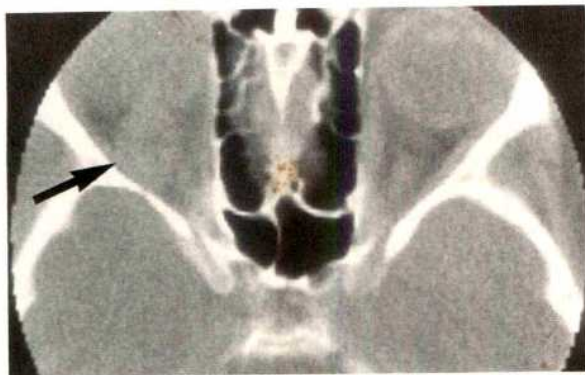


Figure 3. Case 4. Unenhanced axial CT scan showing a rounded mass of soft-tissue density (arrow) between the left optic nerve and the lateral rectus muscle.

Coronal inversion-recovery (IR 1500/500/40, strongly T_1 weighted) images showed the lesion to be less homogeneous, but to give a predominantly low signal, indicating a prolongation of T_1 . At surgery, a blood-filled cyst was evacuated; biopsy of its wall showed non-specific fibrous tissue.

Case 4. A 14-year-old boy presented with a 4-day history of painful right proptosis; vision was unaffected. Again, CT showed a non-specific, well defined intraconal mass (Fig. 3). After surgical evacuation of a blood-containing cyst, recovery was complete. Histological examination was compatible with uncomplicated haemorrhage.

Case 5. A 25-year-old man presented after 6 months of painful proptosis, without visual disturbance. On CT, there was a slightly elongated intraconal mass (Fig. 4), and at surgery an encysted collection of blood was removed. His symptoms have not recurred.

Case 6. In 1970, aged 4 years, the patient presented with acutely painful left proptosis. Skull radiographs, carotid angiography and orbital venography showed no abnormality, but an intraconal blood cyst was found at surgery. This recurred soon after evacuation, but the boy was free of symptoms until 1980, when he returned complaining of 3 days of proptosis. Visual acuity on the affected side had been normal but was now 6/18. In view of the previous history, the rounded intraconal mass revealed by CT was managed conservatively, with full recovery.

Case 7. A 26-year-old woman presented with 1 day of painful proptosis, visual acuity on the left being reduced to 6/18. Computed tomography showed a well defined, rounded mass of greater density than brain in the anterior half of the intraconal, retrobulbar space (Fig. 5). Based on experience with the preceding cases, management was again conservative, and the patient recovered fully.

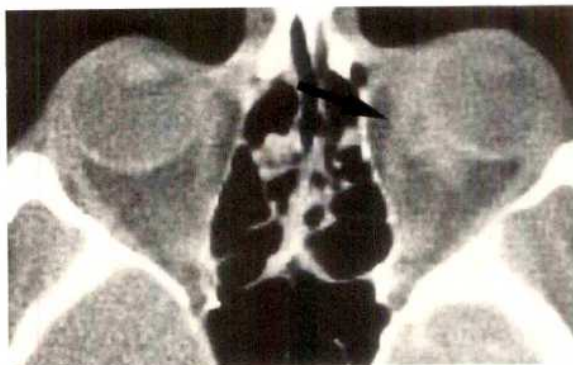


Figure 4. Case 5. Unenhanced axial CT scan. An elongated, well defined mass of soft-tissue density (arrow) lies just behind the globe, extending from the medial rectus to the optic nerve.

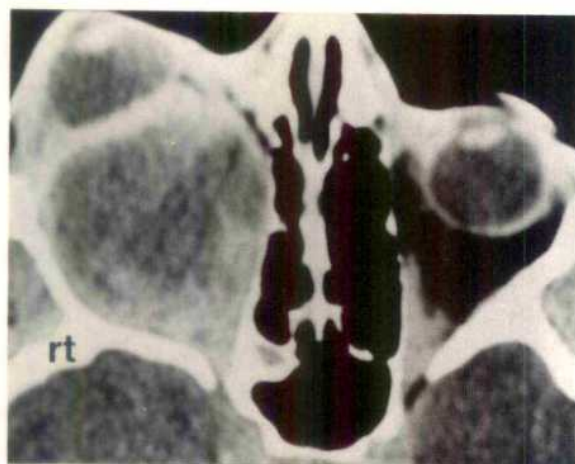
Case 8. A 15-year-old girl was found in 1980 to have a right optic nerve glioma, which was debulked twice up to 1985, and in December 1986 the eye was enucleated because of marked proptosis. During the course of her treatment she twice developed acute proptosis: in February 1985, when a considerable amount of blood was aspirated from the retrobulbar space, and in February 1986, when CT and MRI were performed. The former revealed a large, inhomogeneous lesion with an enhancing wall; on inversion-recovery (strongly T_1 weighted) MR images the mass was of uniformly low signal, whereas with T_2 weighting (SE 1500/60) the signal was high (Fig. 6). Operation showed a large cavity filled with what appeared to be old blood, but histological examination of its posterior wall showed some glioma cells.

Discussion

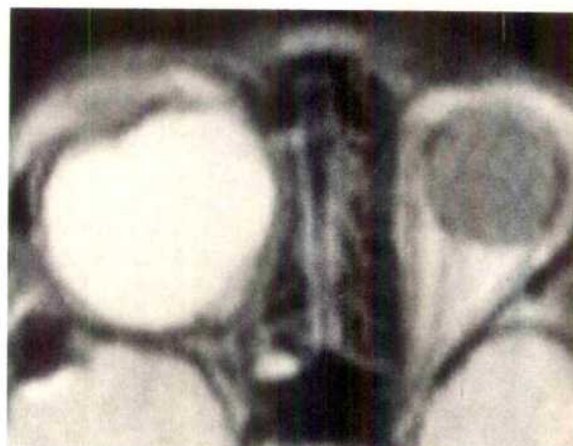
Intraorbital haemorrhage can occur spontaneously, or secondary to a known cause, including trauma and



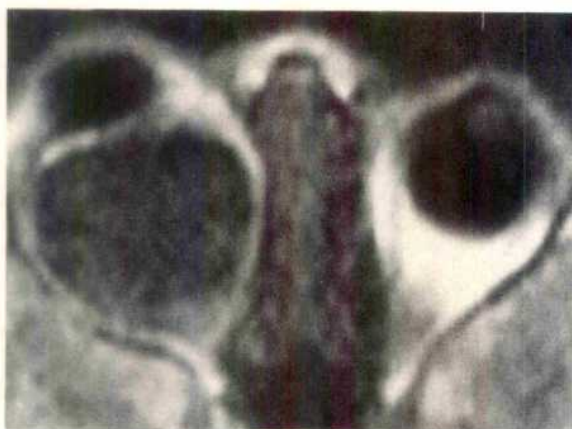
Figure 5. Case 7. Unenhanced axial CT scan showing a rounded mass, denser than brain, in the left intraconal space, just behind the globe.



(a)



(c)



(b)

Figure 6. Case 8. (a) Enhanced axial CT scan. A very large mass, of predominantly low density, fills the right retrobulbar space, causing gross proptosis; there is some contrast enhancement around its margins, especially posteriorly. (b, c) IR 2060/500/40 and SE 1500/60 images: the mass appears of uniform low and very high intensity, respectively, with a suggestion of material closer in intensity to brain posteromedially.

blood dyscrasias (Krohel & Wright, 1979) or, because the orbital veins have no valves, to sudden increase in venous pressure, as occurs during a Valsalva manoeuvre (Katz & Carmody, 1985) or venous compression for orbital phlebography (Safer & Guibor, 1975). Primary orbital lesions, including varices, arterio-venous malformations and vascular tumours, can also bleed. Blood products that are not rapidly resorbed can remain as a cystic accumulation of fluid whose capsule is formed by the orbital connective tissues, a haematic cyst. The cyst may enlarge, because of fibrinolysis and recurrent bleeding (Pearson et al, 1986; Shapiro et al, 1986).

Previous reports concern haematic cysts arising beneath the periosteum of the floor or roof of the orbit, where the blood is surrounded by the periosteum and, if chronic, can cause resorption of adjacent bone (Siegel et al, 1982; Milne et al, 1987). In the present series, the lesions were shown by imaging procedures to be intraconal, and all the patients were children or young adults.

In a careful anatomical study, Koorneef (1977) showed radial fibrous connective tissue septa in both the

intra- and extraconal portions of the orbital fat. These tend to be less obvious in older individuals, in whom retrobulbar blood tends to track forwards to the conjunctiva, thereby facilitating diagnosis. We have previously postulated that in young patients the better developed septa prevent the spread of blood, causing the haematoma to become encysted, and accounting for the observation of intraconal haematic cysts in children and young adults (Krohel & Wright, 1979). This is borne out by the imaging procedures reported here, which showed in every case a rounded, well defined, intraconal lesion indistinguishable from a benign neoplasm; in most of the patients, the cyst did not even fill the intraconal space.

Given the events that preceded the second presentation in Case 6, and the characteristic history in Case 7, together with the typical CT findings and spontaneous resolution of symptoms and signs in both patients, we consider that alternative diagnoses are sufficiently improbable as to warrant their inclusion in this series. The second of these cases, the only lesion examined by CT in the acute phase, showed high

density, indicative of its haemorrhagic nature, and this was also true of the cyst in Case 3, examined 3 weeks after the onset of symptoms; the radiographic density of the remaining subacute or chronic cysts was in the non-specific soft-tissue range.

Not all the patients described a rapid onset of proptosis or acute pain, but awareness that when in a young person these are associated with a focal, rounded, intraconal mass on CT, an uncomplicated haemorrhage is a strong possibility, which will mean that surgery can be avoided. The results of imaging thus play a positive role in management, although operative exploration may still be required in atypical presentations. Familiarity with the likely clinical diagnosis in Cases 6 and 7, together with the CT findings now recognizable as characteristic of these cysts, allowed conservative management, despite the temporary visual disturbance.

Neither radiological investigation nor surgery showed any evidence of an underlying lesion, such as a venous malformation, in any patient apart from Case 8, the patient with the optic nerve glioma. We have seen acute retrobulbar haemorrhage in the course of treatment of other patients with this condition, but diagnostic imaging procedures were not carried out.

We are unaware of previous descriptions of orbital haematic cysts examined by MRI. The findings are somewhat surprising: in the brain, the products of haemorrhage characteristically have a short T_1 , due to the presence of methaemoglobin, and give high signal on images with T_1 or T_2 weighting. During the acute or subacute phase, this is often associated with low signal on T_1 weighting due to deoxyhaemoglobin; subsequently low signal may be generated on both T_1 - and T_2 -weighted images by haemosiderin, seen characteristically at the margins of the clot (Gomori et al, 1985). In both cases illustrated here, the contents of the

cyst gave low signal on T_1 -weighted images, with no suggestion of associated low signal on T_2 weighting, but at operation soon afterwards the contents of the cyst appeared frankly bloody. These observations, in common with others we have seen in which blood within the orbit did not give the expected signal abnormalities, suggest that the evolution of orbital haematomas may differ from that seen in the brain; this possibility is under investigation.

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The diagnosis of tumours involving the parapharyngeal space by computed tomography

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Abstract. Tumours arising within or adjacent to the parapharyngeal space are usually large at presentation and present difficulties in the choice of surgical approach. The findings on contrast-enhanced computed tomography (CT) of 30 patients with mass lesions in this region are presented. Contrast-enhanced CT can provide reliable information regarding the size and extent of a mass, its site of origin and likely histological type, as well as its relationship to surrounding neurovascular structures.

The parapharyngeal spaces (PPS) are bilateral, fat-containing tissue planes that extend from the skull base to the hyoid bone. Clinical examination of the PPS is difficult as they lie deep to the muscles of mastication, mandible and parotid glands. Only a mass of considerable size will cause a visible bulge or palpable abnormality of the lateral pharyngeal wall or external neck (Som et al, 1981).

The findings on contrast-enhanced computed tomography (CT) of 30 mass lesions arising within, or related to, the PPS are presented; the pathological diagnosis was confirmed in most cases. It is possible to diagnose the tissue of origin of a mass and likely histological type in the vast majority of cases. This information will influence treatment options, the site of biopsy and, if surgery is decided upon, the exact surgical approach to be employed.

Anatomy

The PPS is the dominant fascial space of the naso- and oropharynx. It consists of a fat-filled cleft in the shape of an inverted triangle extending from the skull base to the floor of the mouth. The PPS diverges away from the mucosal surface of the pharynx near the lower pole of the tonsil (Fig. 1). The relationships of the PPS are best appreciated in the axial plane (Fig. 2). The medial boundary is the lateral wall of the pharynx consisting of deglutition muscles, the lymphoid tonsils and the pharyngeal mucosa. The antero-lateral border consists of the pterygoid muscles and laterally lies the deep lobe of the parotid gland. Posterior to the PPS is the styloid process and its attached musculature and the carotid space is posterior to the styloid process. The pre-vertebral space is situated on either side of the midline posterior to the retropharyngeal space and pre-vertebral muscles. The carotid space contains structures of critical importance: the internal jugular vein, the internal carotid artery, the cervical sympathetic chain, the vagus nerve and cranial nerves IX, XI and XII, which leave the space at various levels in the upper neck.

The PPS can act as a conduit for tumour and infection to spread superiorly to the skull base. The

principal skull base foramina lie just outside the superior margins of the PPS. In addition to fat, the PPS contains the pharyngeal venous plexus, the ascending pharyngeal and maxillary arteries and branches of the mandibular division of the trigeminal nerve. Asymmetry of size of the PPS is a normal variant because of a variable amount of tonsillar lymphoid tissue causing asymmetrical thickness of the lateral pharyngeal walls (Muraki et al, 1983). However, the margins of the PPS as seen on CT should always be smooth and clearly defined and the antero-lateral, lateral and posterior margins should be symmetrical.

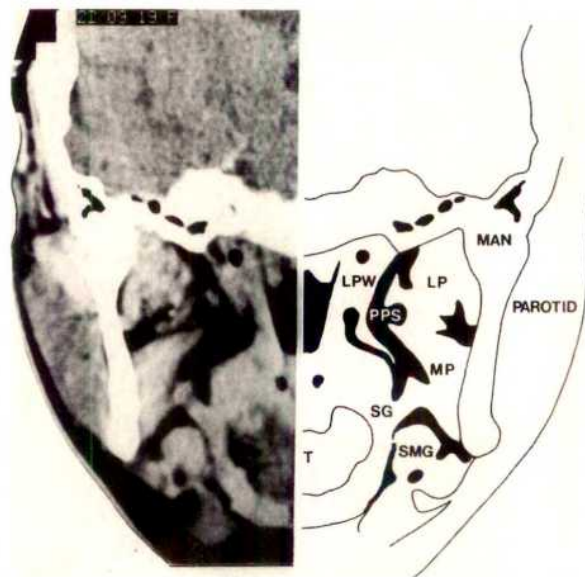


Figure 1. Normal coronal anatomy of the PPS. MAN=mandible; LP=lateral pterygoid; MP=medial pterygoid; PPS=parapharyngeal space; LPW=lateral pharyngeal wall; SG=styloglossus; SMG=submandibular gland; MASS=masseter; S=styloid process; CS=carotid space.

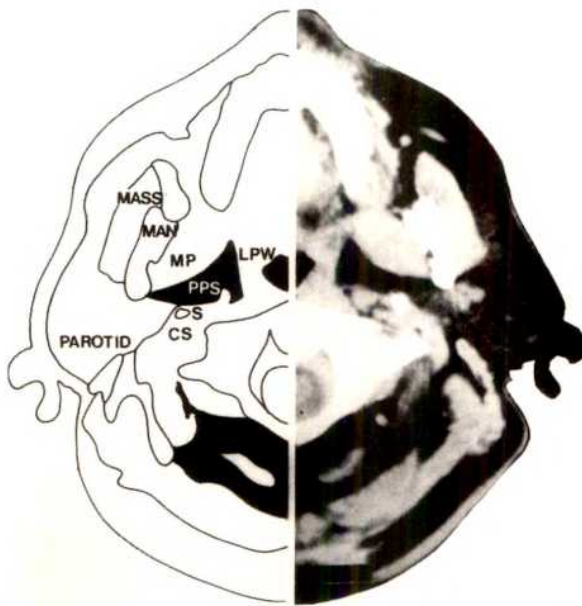


Figure 2. Normal axial anatomy of the PPS. Labels as for Fig. 1.

Materials and methods

Thirty patients with the clinical diagnosis of a mass in the deep structures of the neck above the hyoid bone or unexplained suprahyoid lymphadenopathy were examined by contrast-enhanced CT. The scans were obtained using a Philips Tomoscan 350 on 60/TX. If the mass was palpable, a single, axial slice was made through the main bulk of the lesion to determine the attenuation value for comparison with the contrast-enhanced scan. Contiguous 6 mm or 5 mm axial sections were performed from the skull base to the hyoid bone. In patients with dental amalgam fillings, a semi-axial projection was employed with 20° cranial angulation of the gantry to avoid artefacts. Coronal scans were performed on larger lesions to delineate better the superior and inferior extent of the lesions with reference to the skull base and hyoid bone, respectively. A bolus of 50 ml of iohexol (300 mg I/ml) was given intravenously prior to scanning. This was followed by a further 50 ml of the same contrast medium or 200 ml of a drip infusion of iohexol (140 mg I/ml) during the rapid scanning sequence.

To evaluate the site or origin of a mass and where possible to predict the likely histological type, the following criteria were used.

- (1) The direction of displacement and resultant deformity of the PPS.
- (2) The direction of displacement of adjacent structures, especially the styloid process and the contents of the carotid space.
- (3) Whether there appeared to be incorporation of the internal jugular vein and internal carotid artery into the mass.

- (4) The vascularity of the mass as determined by contrast-enhanced CT.
- (5) Features to suggest malignancy such as irregular margins with infiltration of surrounding structures, loss of fat planes rather than displacement, bone destruction and lymphadenopathy.

Results

Following evaluation of the CT scans, the 30 lesions were grouped according to their site of origin with reference to the PPS.

Medial

Eight patients were included in this group. The PPS was indented on its medial aspect or displaced laterally according to the size of the mass arising in its medial boundary (Fig. 3). All cases were either non-Hodgkin's lymphoma (NHL) or squamous cell carcinoma arising primarily within the nasopharyngeal wall or by spread from contiguous mucosal surfaces. Non-Hodgkin's lymphoma involved Waldeyer's ring diffusely, the nodes were large and not necrotic (Fig. 4). Involvement of the pharyngeal wall by squamous cell carcinoma could be subtle, manifesting as slight, asymmetrical thickening of the pharyngeal wall. However, such tumour involvement can only be distinguished from asymmetrical wall thickening as a normal variant by biopsy or the presence of enlarged or necrotic lymph nodes in the appropriate drainage area (Fig. 5). Other squamous cell carcinomas involving the medial border showed more diffuse spread and the exact site of origin could not be predicted.

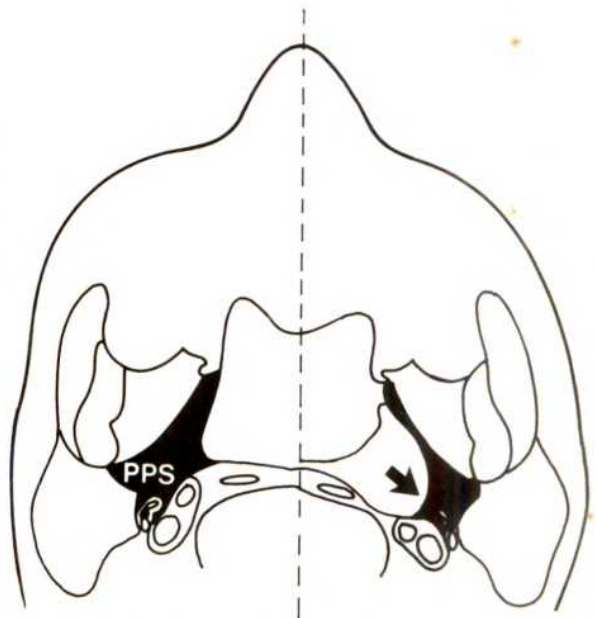


Figure 3. Medial. Masses arising in the lateral pharyngeal wall will displace the PPS laterally.

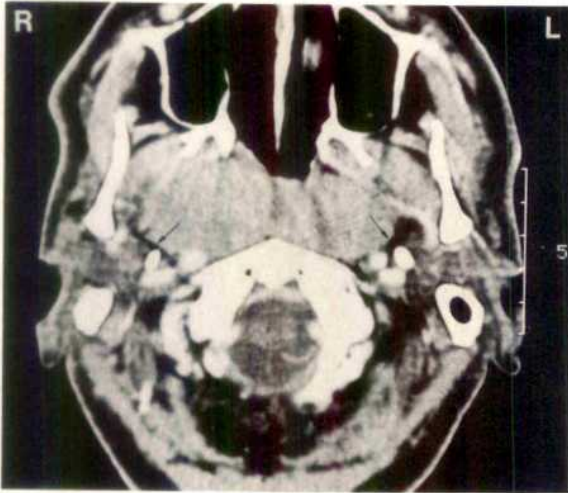


Figure 4. Medial. Enlarged lymph nodes due to non-Hodgkin's lymphoma arising from Waldeyer's ring have displaced the PPS laterally (arrows).

Antero-lateral

The lesions indented the PPS from the antero-lateral aspect displacing the PPS postero-medially (Fig. 6). Included in this group of three cases were developmental hypertrophy of the medial pterygoid muscle in a patient with asymmetrical, masseteric hypertrophy (Fig. 7) and a case of involvement of the pterygoid muscles by extensive squamous cell carcinoma (Fig. 8).

Lateral

All nine patients in this group had lesions arising within the parotid gland. These masses spread, from the

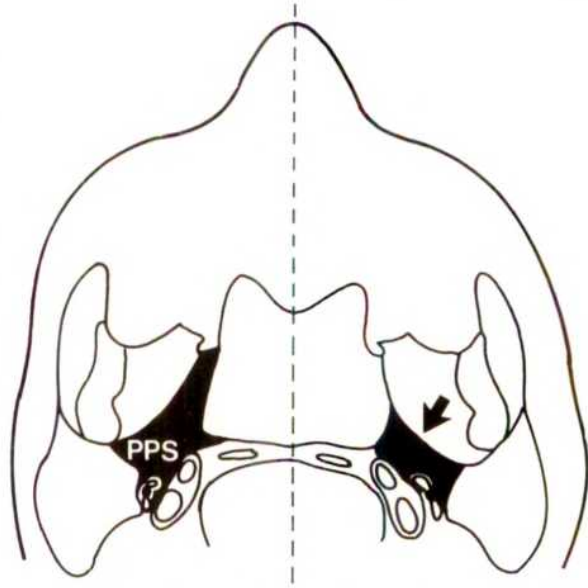
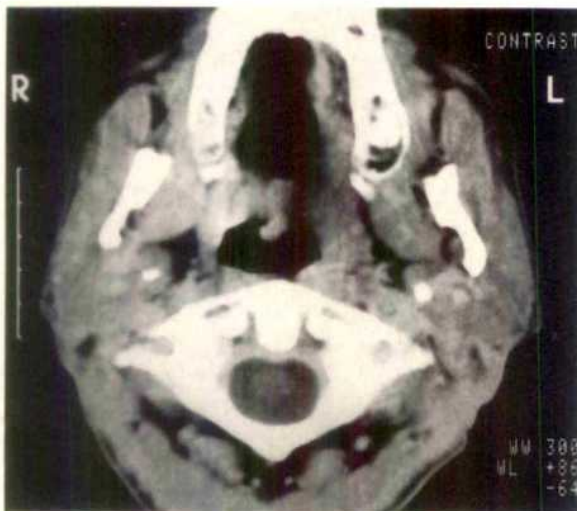


Figure 6. Antero-lateral. The PPS is displaced postero-medially by a mass arising antero-laterally.

deep lobe of the parotid medially, anterior to the styloid process with variable lateral displacement of the PPS (Fig. 9). Distinction could not always be made on radiological grounds between benign and malignant tumours. Benign tumours were well defined and of similar density to the normal gland (Fig. 10).

Posterior

There were five lesions in this group, which can be subdivided into masses arising laterally within the



(a)



(b)

Figure 5. Medial. (a) There is asymmetry between the lateral pharyngeal walls. Biopsy of the thicker left wall revealed squamous cell carcinoma. (b) There is extensive lymphadenopathy in both jugulo-digastric and the left submandibular groups. Many nodes show necrosis, typical of squamous cell carcinoma.

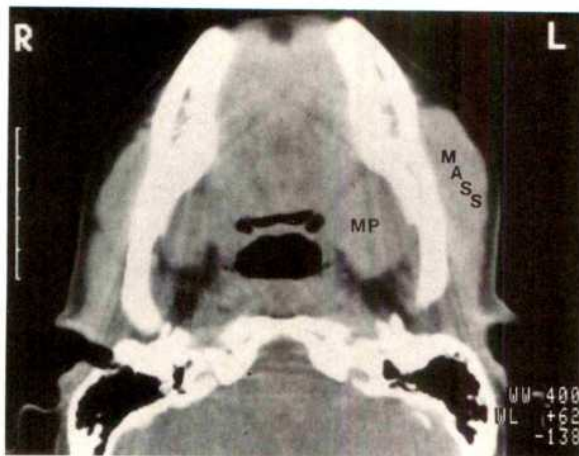


Figure 7. Antero-lateral. Asymmetrical developmental hypertrophy of the medial pterygoid (MP) and masseter (MASS) muscles.

carotid space or medially from the retropharyngeal/pre-vertebral space.

Carotid space. Carotid space masses displace the styloid process and PPS anteriorly (Fig. 11); they may be vascular, neural or nodal in origin. Neural tumours included a solitary paraganglionoma and two Schwannomas and these lesions could be distinguished by characteristic enhancement patterns and vascular displacement or incorporation. Nodal enlargement was due to lymphoma or squamous cell carcinoma.

Retropharyngeal/pre-vertebral. The retropharyngeal lesions were caused by lymphadenopathy due to lymphoma. There were two pre-vertebral lesions: tuberculous involvement of C1 vertebra extending



Figure 8. Antero-lateral. An extensive squamous cell carcinoma probably arising within the right lateral pharyngeal wall has involved the pterygoid and masseter muscles, mandible and antrum and has extended posteriorly to obliterate the PPS.

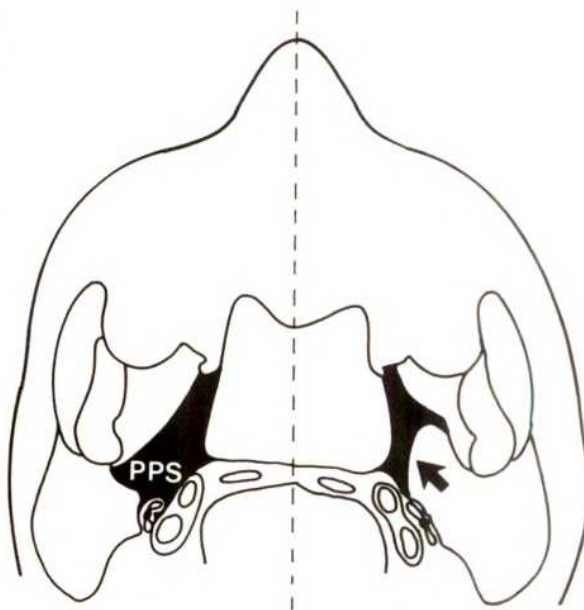


Figure 9. Lateral. A mass arising in the deep lobe of the parotid will extend medially, anterior to the styloid process, displacing the PPS laterally.

anteriorly to form a pre-vertebral abscess (Fig. 12) and an intradural, extramedullary meningioma in the same region with anterior spread.

Discussion

Tumours arising within or adjacent to the PPS are uncommon and there are only a few series of cases reported in the literature (McIlrath et al, 1963; Work & Hybels, 1974; Som et al, 1984; Schoss et al, 1985). These tumours, however, represent a considerable surgical

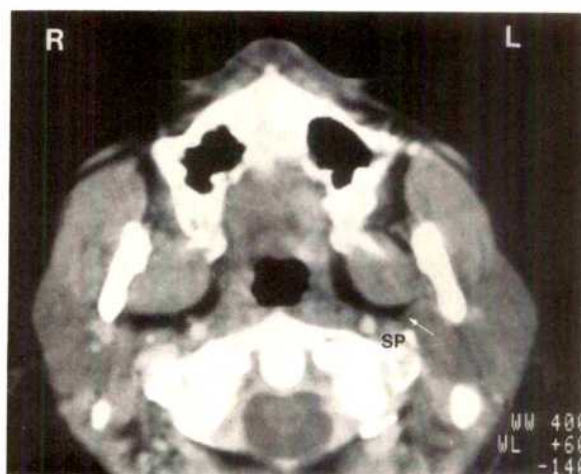


Figure 10. Lateral. There is a benign cystic tumour that shows slight extension into the PPS, passing anterior to the styloid process (SP).

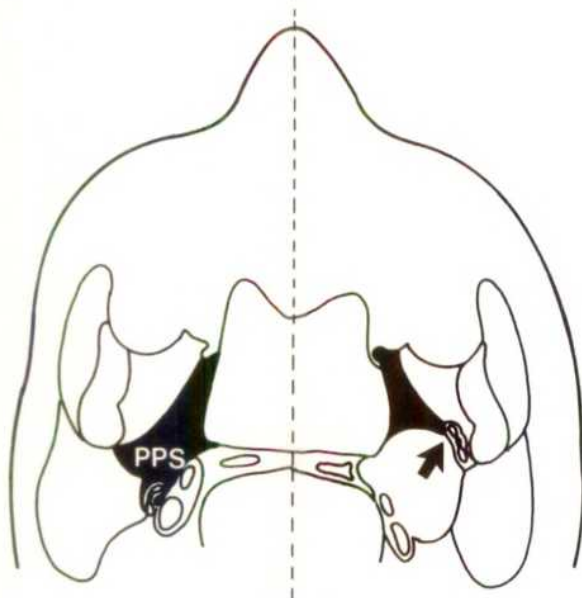


Figure 11. Posterior. The PPS and styloid process are displaced anteriorly by a mass arising with the carotid space.

challenge as many are large at presentation and access for their safe and complete removal is difficult. Lesions arising within or adjacent to the PPS are usually slow growing and clinically asymptomatic. The most common presentation is of a visible or palpable mass of the lateral pharyngeal wall with or without an external mass anterior to or below the tragus of the ear (Schoss et al, 1985).

Arteriography was for many years the mainstay of radiological diagnosis. Tumour vascularity and vessel

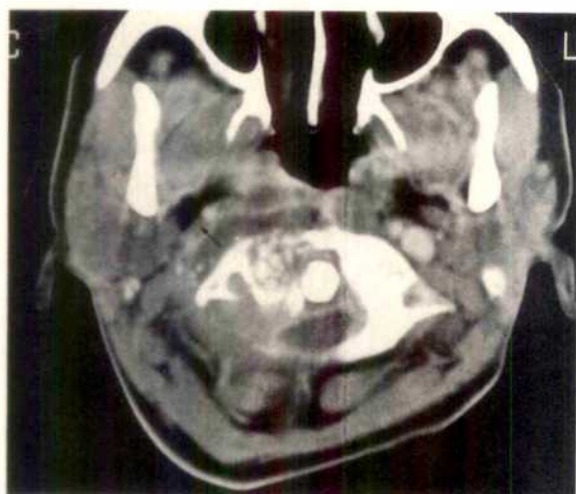


Figure 12. Posterior. There is tuberculous involvement of the right side of C1 with anterior extension to produce a retropharyngeal abscess that has displaced the PPS anteriorly (arrow).

Table 1. An analysis of the 30 cases according to their tissue of origin

Tissue of origin	Number of cases
Developmental	2
Vascular	1
Infection	1
Lymphoma	7
Squamous cell carcinoma	7
Salivary gland tumours	8
Neural	4
Total	30

displacement can be demonstrated and this occasionally indicates tumour type and site of origin (Silver et al, 1984). However, carotid angiography is an invasive procedure, which supplies limited or no information concerning the relationship of the tumour to surrounding structures and tissue planes of the head and neck.

Computed tomography demonstrates the size and extent of a mass and its relationship to surrounding structures. The direction of displacement of the PPS fat-plane, styloid process and carotid space vessels allows the site of origin of a mass to be accurately predicted, although this distinction is not always possible with large lesions or those of an aggressive nature that infiltrate rather than displace fat-planes.

A wide variety of histological types of tumour can occur within or adjacent to the PPS (Table 1). Contrast-enhanced CT is an accurate means of predicting the likely histology when the following characteristics of the tumour are evaluated.

Site of origin

Specific tumours tend to arise in each of the four borders of the PPS. Salivary gland neoplasms predominate in the parotid gland, which forms the lateral border, neurogenic tumours occur posteriorly and squamous cell carcinomas and lymphomas are seen mainly in the medial and posterior compartments.

Likelihood of malignancy

Indicators of malignancy include irregular tumour margins and spread into surrounding tissues and fat-planes. Squamous cell carcinoma, in addition, may demonstrate enlarged, necrotic lymph nodes in the appropriate drainage areas (Fig. 8). In contrast, lymphoma usually presents as relatively well defined enlarged masses of lymphoid tissue in Waldeyer's ring (Fig. 4). Malignant parotid tumours are uncommon, but when small they may appear identical to benign lesions on CT, being well defined with none of the previously described features of malignancy (Som et al, 1981).

Contrast-enhancement pattern and the effect on the carotid sheath vessels

Evaluation of neural tumours of carotid sheath origin is dependent on these factors (Silver et al, 1984).

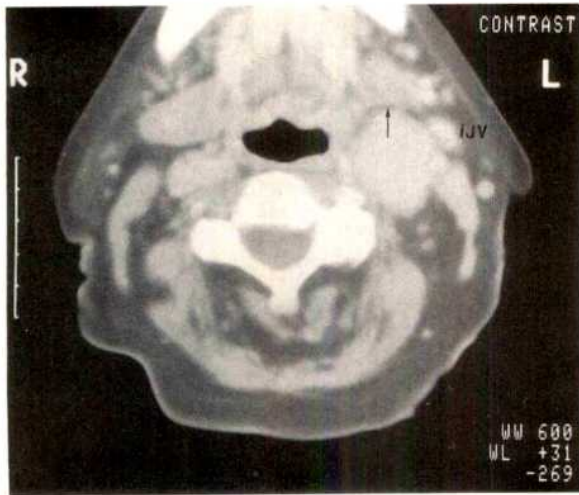


Figure 13. Axial CT scan just above the hyoid bone. The PPS is displaced anteriorly (arrow) by a homogeneously enhancing paraganglionoma. The internal jugular vein (IJV) is displaced laterally and the internal carotid artery is incorporated into the mass.

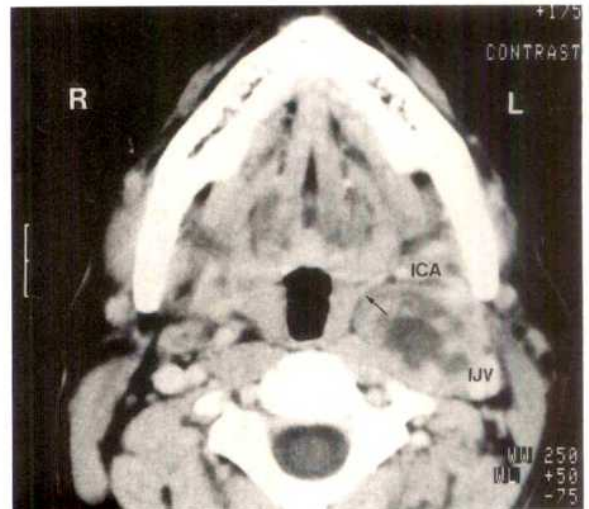


Figure 14. Suprahyoid axial CT scan. The internal carotid artery (ICA) and PPS (arrow) are displaced antero-medially by a Schwannoma, which exhibits the typical mottled enhancement pattern.

Neurogenic tumours above the hyoid bone most commonly arise from the vagus nerve and include paraganglionomas of nerve cell origin and Schwannomas of nerve sheath origin. Paraganglionomas are extremely vascular lesions and show homogeneous enhancement with incorporation of surrounding vessels (Fig. 13). In contrast, Schwannomas displace the internal carotid artery medially, separating it from the internal jugular vein. The vascularity of Schwannomas is variable but they usually exhibit a mottled enhancement pattern (Fig. 14).

Modifications of the basic technique of contrast-enhanced CT have been advocated to increase the diagnostic yield of the study. The combined CT-sialogram is an effective means of differentiating deep-lobe parotid tumours from extraparotid PPS masses (Som et al, 1981). However, with modern generation CT scanners the location of a PPS mass can be determined from the direction of displacement of the PPS fat-plane in the vast majority of cases without the need to perform a sialogram.

Som et al (1984) evaluated PPS masses by dynamic CT. The main advantage of this technique is the ability to distinguish between a paraganglionoma and those small to moderate sized Schwannomas that show marked homogeneous enhancement. The two tumours have very different attenuation-versus-time curves; the paraganglionoma has a sharp initial peak paralleling the arterial and venous curves as compared with the slowly rising curve of a Schwannoma. Selective carotid angiography is our preferred technique in this situation, providing a clear distinction between these two lesions and a more complete demonstration of the vascular anatomy for the surgeon.

There are several possible surgical approaches to the PPS. A transcervical approach is usually employed with or without a superficial parotidectomy and division of the mandible to improve access and provide better exposure of the neurovascular anatomy. Occasionally, this is supplemented with an intraoral incision to aid mobilization of the tumour. Masses arising within or adjacent to the PPS can be fully evaluated with contrast-enhanced CT, allowing an appropriate surgical procedure to be employed.

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Comparison of techniques for thallium-201-technetium-99m parathyroid imaging

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Abstract. It is impracticable to compare the variety of techniques advocated for thallium-technetium (Tl-Tc) subtraction parathyroid imaging by repeated studies in patients. We therefore carried out studies using a phantom assembly to simulate thyroid and parathyroid in the neck, containing activities of $^{99}\text{Tc}^m$ and ^{201}Tl similar to those likely to be present in patient imaging. An initial study of imaging protocol confirmed that correction for scatter from $^{99}\text{Tc}^m$ in the ^{201}Tl window usefully improved the image. After making a preliminary selection of gamma cameras and collimators it was found that the GE Maxicamera 400T just visualized the 0.3 g "parathyroid" in a 5 min image with the pinhole collimator and 6 mm insert (A). It performed slightly less well with the HR converging collimator (B) and only marginally better with the 4 mm insert (C), but this is unduly slow unless it is placed close enough to limit the field of view unacceptably. The Siemens Orbiter 75 ZLC with special thyroid collimator (D) gave results similar to (A), is convenient for positioning the patient and is very suitable for parathyroid imaging.

A considerable number and variety of techniques have been advocated for thallium-technetium (Tl-Tc) subtraction parathyroid imaging (Ferlin et al, 1981; Young et al, 1983; Okerlund et al, 1984; Basarab et al, 1985; Winzelberg & Hydovitz, 1985; Chatterton et al, 1987; Blake et al, 1988) and it is impracticable to compare their relative merits by repeated studies in the same patient. We therefore devised a phantom assembly to simulate the size of the structures and the distribution of activity in parathyroid and thyroid in a patient's neck in order to provide data for comparison of imaging techniques.

Methods

Phantom assembly

The phantom assembly is illustrated in Fig. 1. The neck was simulated by a plastic container filled with approximately 1.5 litres of water containing 2 MBq $^{99}\text{Tc}^m$ or 2 MBq ^{201}Tl or both. The thyroid was simulated by a thin-walled plastic tablet bottle measuring 1.8 cm $\times$ 3.0 cm $\times$ 4.2 cm with a volume of 25 ml. This contained 2 MBq $^{99}\text{Tc}^m$ or 0.25 MBq ^{201}Tl or both.

The parathyroid was simulated by a 2 ml plastic syringe taped below the centre of the "thyroid" and containing ^{201}Tl at a concentration of 0.02 MBq ml $^{-1}$ (twice the concentration of ^{201}Tl in the "thyroid") and in volumes from 0.2 to 0.8 ml. The concentration of $^{99}\text{Tc}^m$ and ^{201}Tl in "neck", "thyroid" and "parathyroid" were derived from data obtained at parathyroidectomy and reported previously (Gimlette et al, 1986); they were approximately those expected from activities administered to a patient of 80 MBq $^{99}\text{Tc}^m$ per-technetate and 80 MBq ^{201}Tl thallous chloride. Identical neck and thyroid phantoms were prepared containing $^{99}\text{Tc}^m$ alone or ^{201}Tl alone or both together in order to compare different imaging protocols (below).

Cameras and collimators

Three gamma cameras, each with a selection of collimators, were available: a GE Maxicamera 400T (crystal thickness 9 mm), a Siemens Orbiter ZLC 75 (crystal thickness 6 mm), and a Siemens (Searle) LFOV (large field of view) (crystal thickness 9 mm). Preliminary studies were carried out using a Picker phantom containing 9 MBq ^{201}Tl imaged for 100 s, which gave approximately the number of counts expected from the phantom assembly, or from a patient, in 5 min, and using several different collimators with each camera.

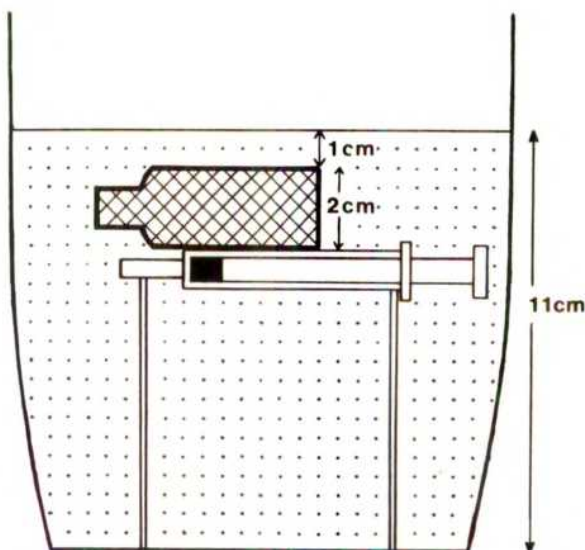


Figure 1. Phantom assembly showing 25 ml plastic bottle ("thyroid") and 2 ml syringe ("parathyroid") mounted in a 1.5 litre container.

The plain, LEHR (low-energy, high-resolution) and LEAP (low-energy, all-purpose), and the converging collimators were placed at 6 cm from the water surface of the phantom and the pinhole collimators at 10 or 6 cm from the surface. The special thyroid collimator (von Gahlen low-energy thyroid collimator) is a straight hole collimator, which projects 3 cm from its housing and was placed at 3 cm; it has a rectangular field of view 19 cm $\times$ 16 cm. One side has a concavity, which comfortably accommodates the patient's chin and helps to minimize inadvertent movement during imaging.

Imaging protocols

Three imaging protocols were simulated using the GE Maxicamera II with the converging LEHR collimator that we had generally been employing for patient imaging.

In the first protocol, $^{99}\text{Tc}^{\text{m}}$ was given first (neck and thyroid phantoms with $^{99}\text{Tc}^{\text{m}}$ alone imaged first) followed by ^{201}Tl (neck and thyroid phantoms then imaged with $^{99}\text{Tc}^{\text{m}}$ and ^{201}Tl together, with "parathyroid" in place). Scatter from $^{99}\text{Tc}^{\text{m}}$ was subtracted from the ^{201}Tl image before normalization and subtraction of the thyroid image.

In the second protocol, ^{201}Tl was given first (phantoms with ^{201}Tl alone and "parathyroid" imaged first) followed by $^{99}\text{Tc}^{\text{m}}$ (phantoms with $^{99}\text{Tc}^{\text{m}}$ and ^{201}Tl and "parathyroid"). In this case there is no $^{99}\text{Tc}^{\text{m}}$ scatter in the ^{201}Tl image to be subtracted before normalization and subtraction of the thyroid image.

In the third protocol, $^{99}\text{Tc}^{\text{m}}$ and ^{201}Tl were given together (neck and thyroid phantoms with $^{99}\text{Tc}^{\text{m}}$ and ^{201}Tl and "parathyroid"). In this protocol, no correction for $^{99}\text{Tc}^{\text{m}}$ scatter in the ^{201}Tl image can be made.

With each protocol, the "parathyroid" to be visualized was placed in position (Fig. 1) containing volumes between 0.2 and 0.8 ml. Each image was for 5 min. In the first and second protocols above, as well as

in the subsequent main study, a matrix shift program was employed to correct for any movement, as in a patient study, since positioning of the syringe is not exactly reproducible, in order to ensure precise alignment of the $^{99}\text{Tc}^{\text{m}}$ and ^{201}Tl thyroid images.

Main study

After the above preliminary studies, the most promising combinations of camera and collimator were tested with the phantom assembly, using the first imaging protocol, and with the parathyroid (2 ml syringe) containing 0.2, 0.3, 0.4, 0.5, 0.6 and 0.8 ml (approximately equivalent to parathyroid adenomas of similar mass), each being imaged for 5 min and the results compared visually. After normalization, subtraction of 60–80% of the thyroid image was usually employed, after some trial and error, to obtain optimum visualization. Some studies were carried out in duplicate.

Results

The quality of the images in the imaging protocol and main studies was generally assessed according to whether the "parathyroids" of various sizes in the phantom assembly were not visualized (–), doubtfully visualized ($\pm$) or clearly visualized (+). The appearance of characteristic images is illustrated in Fig. 2.

Cameras and collimators

Assessment was by observing whether the smallest (5 mm) "cold spot" in the Picker phantom was not visualized (–), indistinctly visualized ($\pm$) or clearly visualized (+). The results are shown in Table I, together with the number of counts acquired in 100 s. The Searle camera was excluded because of its slow count rate and the LEHR collimator on the Maxicamera and the converging collimator on the Orbiter were excluded because of their poor resolution.

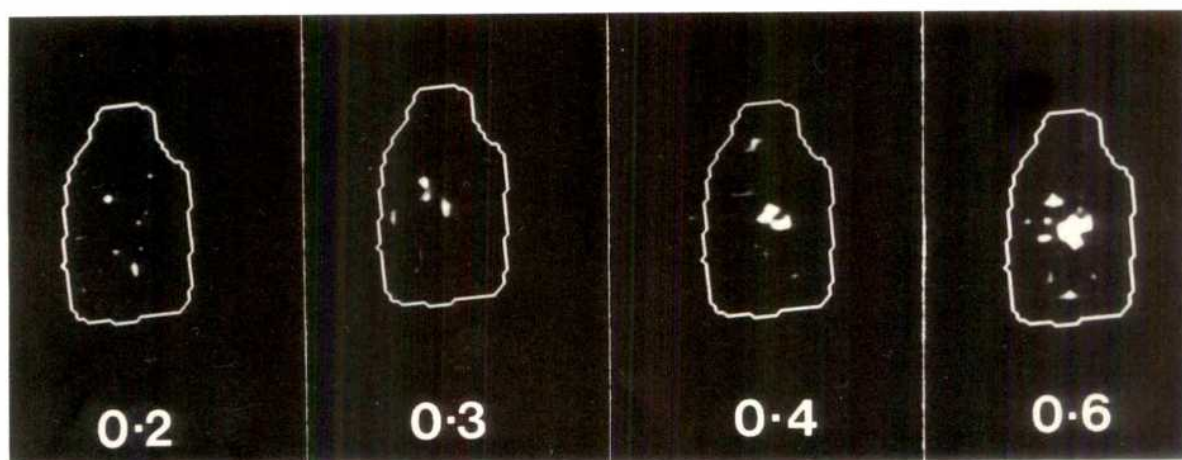


Figure 2. Images showing the area of interest of the "thyroid" with "parathyroids" containing 0.2 ml (not visualized), 0.3 ml (just visualized), and 0.4 ml and 0.6 ml (clearly visualized).

Table I. Cameras and collimators

	Counts ($\times 1000$) in 100 s	Visualization
Maxicamera		
LEHR collimator	213	—
Converging LEHR	309	$\pm$
Pinhole 6 mm insert at 10 cm	122	+
Pinhole 4 mm insert at 10 cm	60	+
Pinhole 4 mm insert at 6 cm	107	+
Orbiter		
Converging LE	370	—
LEAP	194	$\pm$
Thyroid	144	+
Searle		
LEHR	95	$\pm$
Pinhole 6 mm insert at 10 cm	58	$\pm$

Imaging protocol

The results of the three imaging protocols are shown in Table II. It was concluded that there was no clear advantage between the first and second protocols, but the third, without scatter correction, was inferior. The first protocol was adopted for the main study.

Main study

The phantom assembly was imaged using the Maxicamera and Orbiter camera with various collimators using the first protocol and various volumes

Table II. Imaging protocol

	Volume of "parathyroid" (ml)				
	0.2	0.3	0.4	0.6	0.8
$^{99}\text{Tc}^m$ then ^{201}Tl	—	—	+	+	+
^{201}Tl then $^{99}\text{Tc}^m$	—	$\pm$	$\pm$	+	+
$^{99}\text{Tc}^m$ and ^{201}Tl together	—	—	—	+	+

Table III. Main study

	Volume of "parathyroid" (ml)					
	0.2	0.3	0.4	0.5	0.6	0.8
Maxicamera						
Converging	—	$\pm$	+	+	+	
Converging (repeat)	—	—	+		+	+
Pinhole 6 mm at 10 cm	—	$\pm$	+	+		
Pinhole 6 mm at 10 cm (repeat)	—	+	+	+	+	
Pinhole 4 mm at 6 cm	$\pm$	$\pm$	+	+	+	
Orbiter						
LEAP	—	—	—	$\pm$	$\pm$	
Thyroid	—	$\pm$	+		+	
Thyroid (repeat)	$\pm$	$\pm$	+		+	

of "parathyroid" as described. The results are summarized in Table III.

The main study indicated that the Maxicamera with the pinhole collimator and 6 mm insert at 10 cm distance with 5 min imaging is just able to visualize the 0.3 ml "parathyroid", and the converging collimator is slightly less good. The pinhole with 4 mm insert at 6 cm gave only marginal improvement. The Orbiter camera with the special thyroid collimator gave similar results to the Maxicamera with the 6 mm pinhole insert, but the higher count rate produces a less noisy image.

Discussion

The phantom studies described in this paper agree with previously published findings (Gimlette et al, 1986) that the smallest parathyroid likely to be readily visualized by Tc-Tl subtraction imaging is about 0.4 g if its percentage uptake of the administered dose of thallium is average. This uptake, however, is likely to vary considerably, and in a small series of eight subjects the mean parathyroid uptake was $0.018\% \text{ g}^{-1}$, range $0.014\text{--}0.029\% \text{ g}^{-1}$ (Gimlette et al, 1986). Our clinical imaging (Gimlette & Taylor, 1985; Gimlette et al, 1986) had been carried out using the first protocol and the Maxicamera with the converging LE collimator. The phantom studies suggest that some improvement may be possible due to superior resolution with other combinations of gamma cameras and collimators. There are, however, two particular considerations that are important in patient imaging.

Field of view

For the Maxicamera with the converging collimator connected to a computer acquiring in zoom mode with the collimator 6 cm from the skin and parathyroid depth, say 2 cm, the field of view is a square approximately $15 \text{ cm} \times 15 \text{ cm}$. While this technique was routinely used for imaging over 100 patients with positive scans and operative findings, only one had a parathyroid adenoma (in the upper mediastinum) that was on the extreme edge of this field of view, and it would have been missed without an additional scintiphoto of the whole field of view, a circle approximately 32 cm diameter.

The pinhole collimator at 10 cm from the skin will give as field of view at parathyroid depth a circle approximately 15 cm diameter, likely to miss very few parathyroid adenomas. The pinhole at 6 cm from the skin with a 4 mm insert gives marginally improved resolution, but the field of view becomes a 10 cm diameter circle, with a greater risk of missing an aberrant adenoma. The geometry of the pinhole collimator also introduces some non-uniformity and spatial distortion. The special thyroid collimator has a rectangular field of view measuring $19 \text{ cm} \times 6 \text{ cm}$, probably adequate to cover the great majority of sites of adenoma. There is no spatial distortion, and the construction of the collimator simplifies positioning for patient imaging and reduces the likelihood of inadvertent movement.

Image quality

Using doses of 80 MBq of both $^{99}\text{Tc}^m$ pertechnetate and ^{201}Tl thallous chloride, counts of about 300 000 in 5 min are obtained in patients with both radionuclides using the Maxicamera with converging collimator. The alternative camera and collimator combinations described give lower count rates, which leads to more noisy images, the difference appearing more noticeable with patient imaging than with the phantom. Smoothing techniques do not overcome the problem satisfactorily and can lead to misleading images and possible false positives. Summation of 5 min images is sometimes helpful, but it is often impracticable to extend the ^{201}Tl imaging time much over three 5-min periods in rather frail, elderly subjects, which many of the patients are. The use of a larger dose of ^{201}Tl than that generally accepted might be advantageous. Furthermore, studies of thallium activity in the thyroid and parathyroid with time after injection (McKillop et al, 1984; Meikle, Southee, Bantovich, McLaughlin & Hutton, 1988, personal communication) confirm our impression that this decreases at a rate of 1–2% min^{-1} , initially, after a peak at about 5 min, so that extending imaging time becomes less useful.

These two considerations of size of field of view and image quality in patient imaging outweigh the advantages of superior resolution with the pinhole collimator to that of the converging collimator. The special thyroid collimator is in an intermediate position and is a satisfactory compromise. The type of phantom described could have other possible applications and could be used to assess equipment other than that described.

Conclusions

We have more recently studied 40 patients using the Orbiter camera with the thyroid collimator, and have found that the resultant images demonstrated similar image quality with respect to resolution and noise to those obtained from the Maxicamera coupled with the converging collimator. One added advantage of the thyroid collimator is that its design facilitates patient positioning and is helpful in reducing the amount of patient movement between images.

We conclude that imaging with the thyroid collimator is the technique of choice, but that the high-resolution converging collimator is also satisfactory if the thyroid collimator is not available.

A phantom assembly of the type described, or a suitably modified version, and a similar experimental approach may be useful in optimizing imaging techniques for parathyroid localization or other relatively complex imaging procedures.

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Spontaneous abrupt changes in the distribution of ventilation: a cause for apparent mismatching on ventilation/perfusion scintigraphy

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Abstract. A defect seen in the perfusion scan in a region of lung that is normally ventilated is usually interpreted as indicating pulmonary vascular disease. Since the distribution of $^{99}\text{Tc}^m$ macro-aggregated albumin (MAA) represents the distribution of perfusion (Q) only at the time of MAA injection, the assumption is required that the distribution of ventilation (V) remains unchanged between MAA injection and the commencement of imaging. We report the V/Q scintigraphic findings in six patients (including four children), in whom this assumption could not be sustained. Thus ventilation imaged with $^{81}\text{Kr}^m$ was seen to change during image acquisition in lobes that showed perfusion abnormalities. In some, but not all, views the appearances were typical for pulmonary vascular disease, which might easily have been misdiagnosed if the changes in the distribution of ventilation had not announced themselves by occurring during image acquisition. A ventilation image obtained immediately before injection of $^{99}\text{Tc}^m$ -MAA may be useful.

Ventilation (V)/perfusion (Q) lung scanning is accepted as the first-line, non-invasive imaging procedure for pulmonary vascular disease, in particular pulmonary embolism. The appearance of a segmental perfusion defect in a region of lung normally ventilated is highly suggestive of pulmonary vascular disease. Other causes of such V/Q mismatching include bronchogenic carcinoma, pulmonary vasculitis, radiation therapy and, in children, sequestrated lobe and congenital anomalies of the pulmonary arterial tree.

In those institutions using $^{81}\text{Kr}^m$ for ventilation imaging, the standard procedure is first to inject $^{99}\text{Tc}^m$ -labelled macro-aggregated albumin (MAA) with the patient supine and then to image, from the usual projections, the distributions of perfusion and ventilation with the patient erect. Children, however, are usually imaged supine and prone.

An assumption implicit in this approach is that the distribution of ventilation remains constant throughout the imaging sequence and, in particular, between the injection of MAA and the commencement of imaging. In this paper we show that this assumption is occasionally erroneous and illustrate the pitfalls when the distribution of ventilation does not remain constant.

Methods and patients

Four children (boys of 2 months, 2 and 10 years and a 3-year-old girl) and two elderly patients undergoing routine V/Q scintigraphy are described.

Technetium-99m MAA was first injected intravenously, in a dose scaled for body-weight and based on

an adult dose of 80 MBq (minimum 10 MBq) with the patient supine. Ventilation/perfusion scintigraphy in the supine position was commenced within 5 min of MAA injection in posterior, anterior and right and left posterior oblique positions. In the adults, the oblique and posterior images were repeated in the sitting (erect) position. The anterior projections in the children were in the prone positions (with the camera underneath). In each position, the distribution of perfusion was imaged on the $^{99}\text{Tc}^m$ window, followed by the distribution of ventilation using $^{81}\text{Kr}^m$. For each image, 200 000 counts were collected.

The children were imaged in supine/prone positions with a Scintatronix Scintag camera fitted with a high-resolution, low-energy collimator and the adults with an IGE 400A camera fitted with a low-energy, general-purpose collimator.

Case 1 was delivered uneventfully at term. A chest radiograph at 5 weeks of age revealed left upper lobe emphysema. He was admitted for investigation of continuing tachypnoea at 3 months, at which time he looked well and was thriving. Faint, bilateral, respiratory rhonchi were heard. The only abnormality on chest radiography was hyper-inflation of the left upper lobe.

Case 2 is a globally retarded 2-year-old boy who had a lung scan because of persistent elevation of the right hemidiaphragm in the face of severe gastro-oesophageal reflux. He has had numerous chest infections thought to be due to aspiration of gastric contents. On examination, thoracic expansion was impaired but the diaphragm moved normally.

Case 3 is a 3-year-old girl who has left upper lobar emphysema resulting from bronchopulmonary dysplasia, but is now asymptomatic. On examination,

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the trachea was deviated to the right with diminished breath sounds on the left.

Case 4 was referred at 10 years of age for investigation of recurrent pneumonia that had affected all lobes of the right lung at different times since he was 3 years old. At 5 years of age, asthma was diagnosed, but symptoms were minor and did not limit his activity. On examination he was entirely normal. The chest radiograph showed right middle lobe consolidation, which was resolving when repeated after 5 weeks.

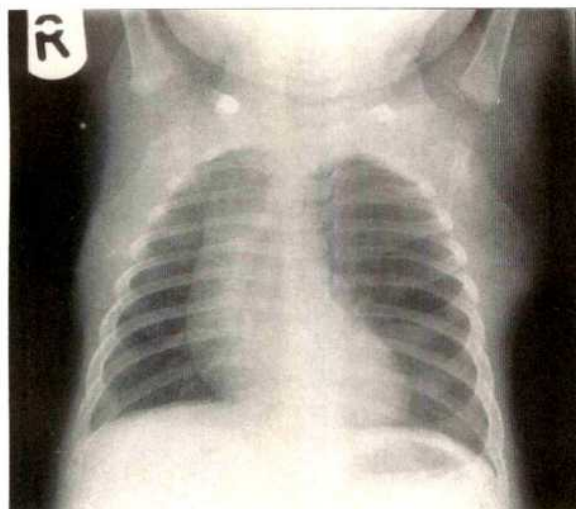
Cases 5 and 6 are elderly and were included in a prospective study aimed at detecting the prevalence of

pulmonary embolic disease in an asymptomatic geriatric population. They had no pulmonary symptoms and chest radiographs showed no significant abnormalities.

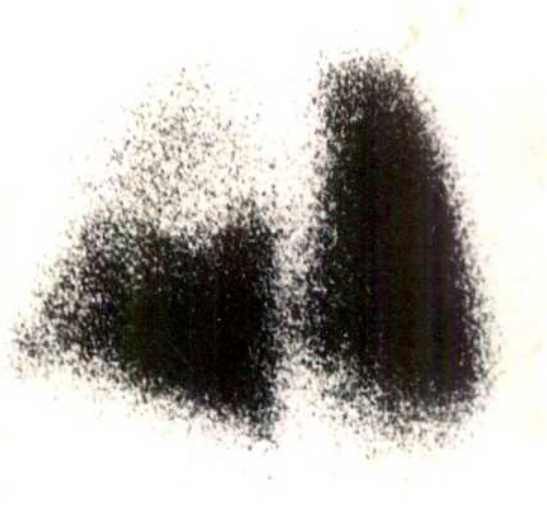
Results

The V/Q images from the six patients are shown in Figs 1–6.

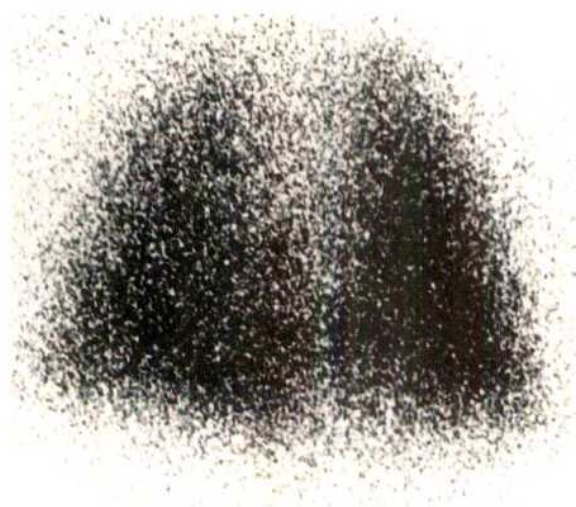
Case 1 (Fig. 1), who has congenital lobar emphysema, had markedly reduced perfusion to the left upper lobe. This abnormal lobe was non-ventilated on the posterior, right posterior oblique and anterior views, but appeared



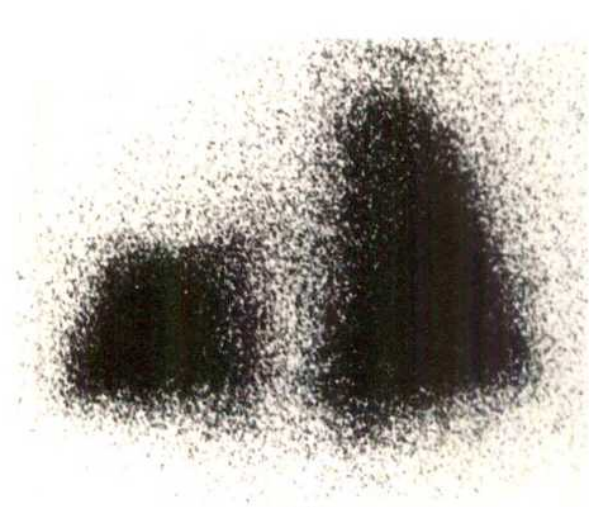
(a)



(b)

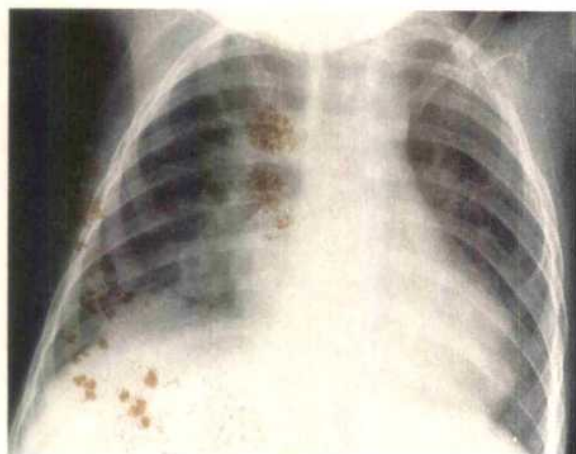


(c)

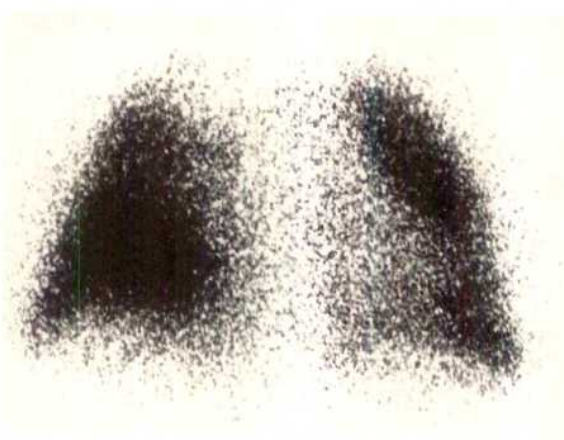


(d)

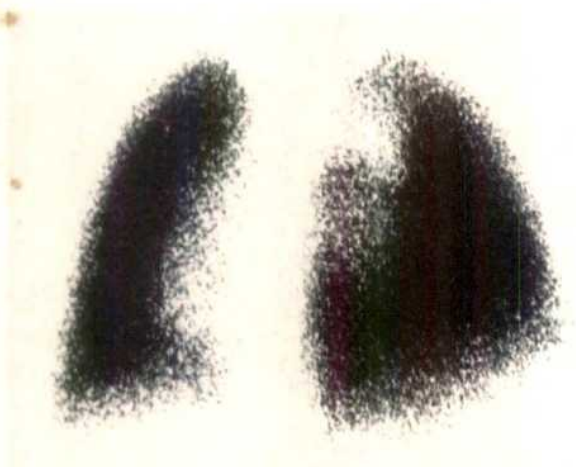
Figure 1. Case 1. (a) Chest radiograph showing increased transradiancy in the left upper lobe. (b) ^{99m}Tc-MAA lung scan in the left posterior oblique view showing markedly reduced perfusion to the left upper lobe. (c) ⁸¹Kr image in the left posterior oblique view showing virtually normal ventilation. (d) ⁸¹Kr image in the posterior view (supine) showing a defect in the left upper lobe, corresponding to the perfusion defect.



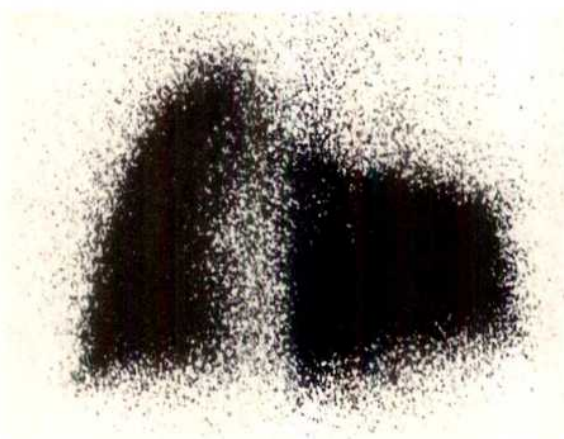
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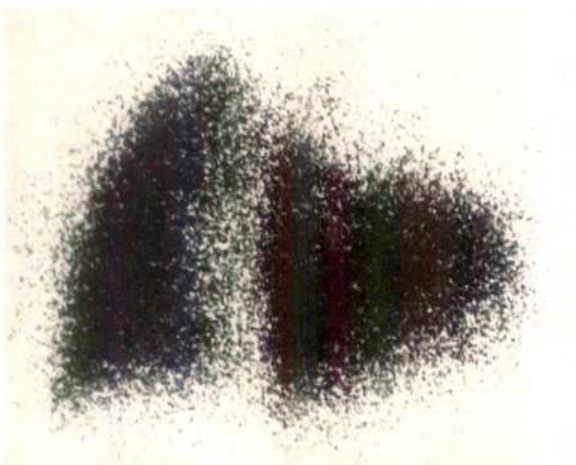
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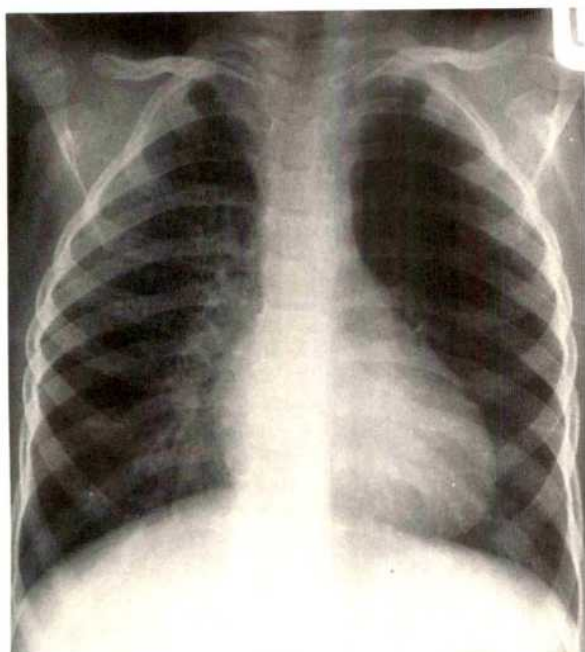


(c)

Figure 2. Case 2. (a) Chest radiograph showing partial collapse/consolidation of the right upper lobe. (b) ⁹⁹Tc-m-MAA lung scan from the right posterior oblique projection showing a defect of perfusion involving the posterior segment of the right upper lobe. (c) ⁸¹Kr-m image in the right posterior oblique projection, in which the patient is 45° decubitus, showing a non-ventilated right upper lobe. (d) ⁸¹Kr-m ventilation image in the anterior (prone) view showing a much smaller defect, now corresponding to the perfusion defect. (e) Repeat of the ⁸¹Kr-m image in the right posterior oblique projection, showing re-appearance of the lobar ventilation defect.

essentially normally ventilated on the left posterior oblique view, the third ventilation image performed.

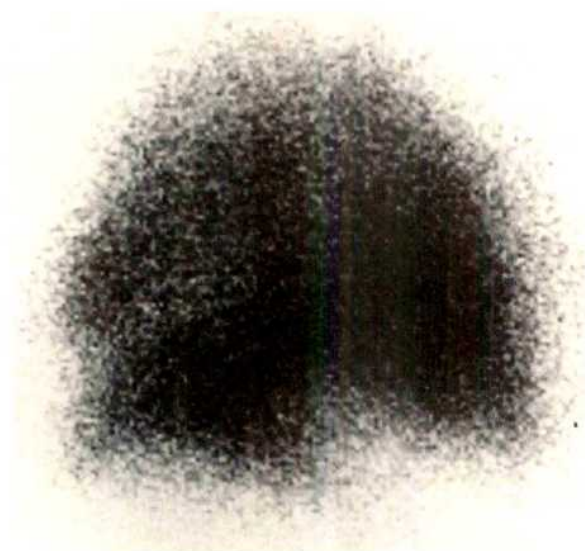
Case 2 (Fig. 2) showed a defect of perfusion to the posterior segment of the right upper lobe corresponding to the abnormality seen on the chest radiograph. This defect appeared to be matched on the ventilation images performed in all positions except the right posterior oblique. In this position there was virtually no ventilation to the entire right upper lobe. On returning the child to this position later during imaging, this



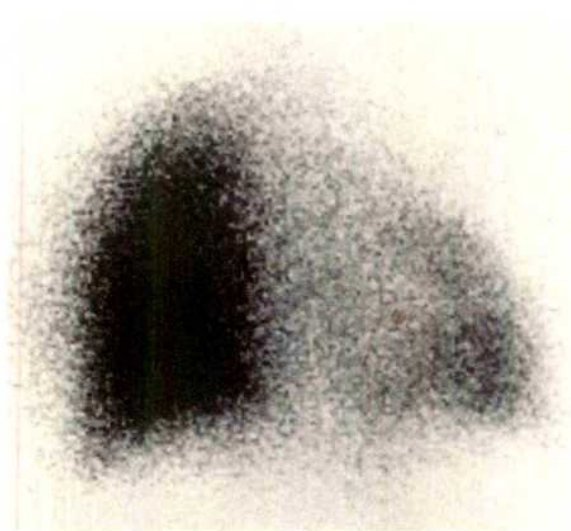
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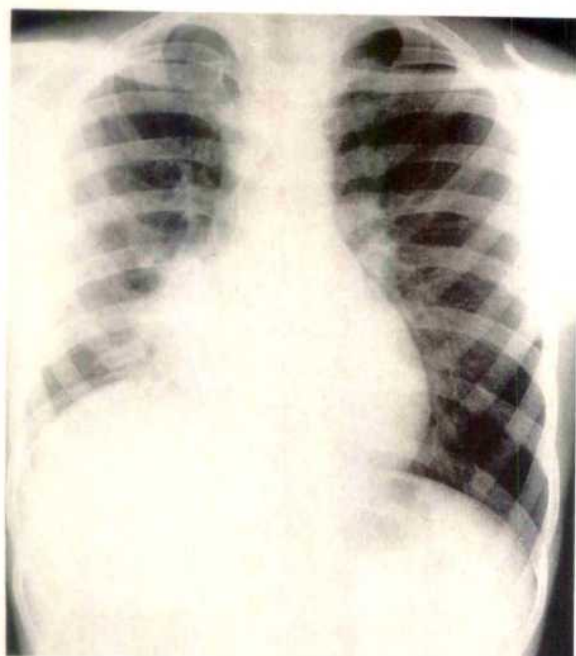


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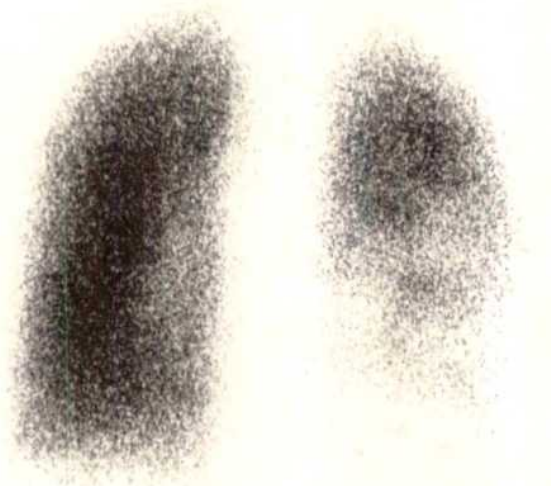
Figure 3. Case 3. (a) Chest radiograph showing increased transradiancy in the left upper zone. (b) $^{99}\text{Tc-m-MAA}$ lung scan in the left posterior oblique projection showing a large defect involving the left upper lobe and part of the lingula. (c) ^{81}Kr image in the left posterior oblique projection is virtually normal. (d) ^{81}Kr image in the anterior (prone) view showing a defect of ventilation in the same distribution as the perfusion defect.

ventilation defect re-appeared. Although in this case the changes in the distribution of ventilation would not have led to a misinterpretation of pulmonary vascular disease, they were reproducible and illustrated an apparent dependence on posture.

Case 3 (Fig. 3) showed a marked diminution of perfusion to the left upper and middle lobes, with some sparing of the middle lobe anteriorly. In the anterior and posterior views, the ventilation and perfusion images were well matched but in the left posterior



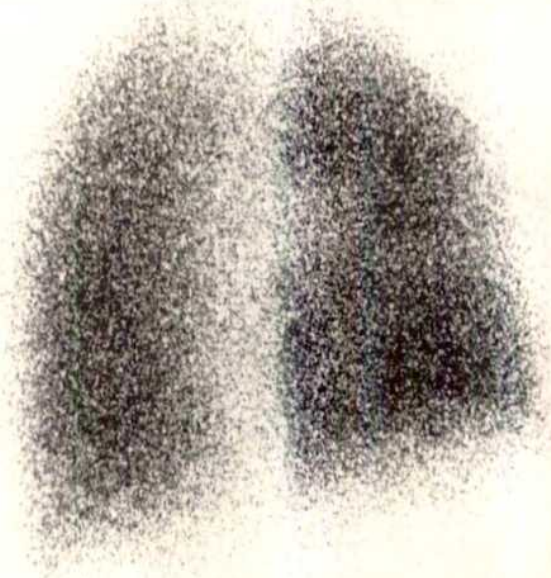
(a)



(b)



(c)



(d)

Figure 4. Case 4. (a) Chest radiograph showing opacification in the right middle lobe. (b) $^{99}\text{Tc}^{\text{m}}$ -MAA scan in the posterior projection showing marked reduction in perfusion to the middle and lower zones. (c) $^{81}\text{Kr}^{\text{m}}$ image in the posterior (supine) projection showing ventilation only in the upper zone. (d) $^{81}\text{Kr}^{\text{m}}$ image in the right posterior oblique view showing virtually normal distribution of ventilation.

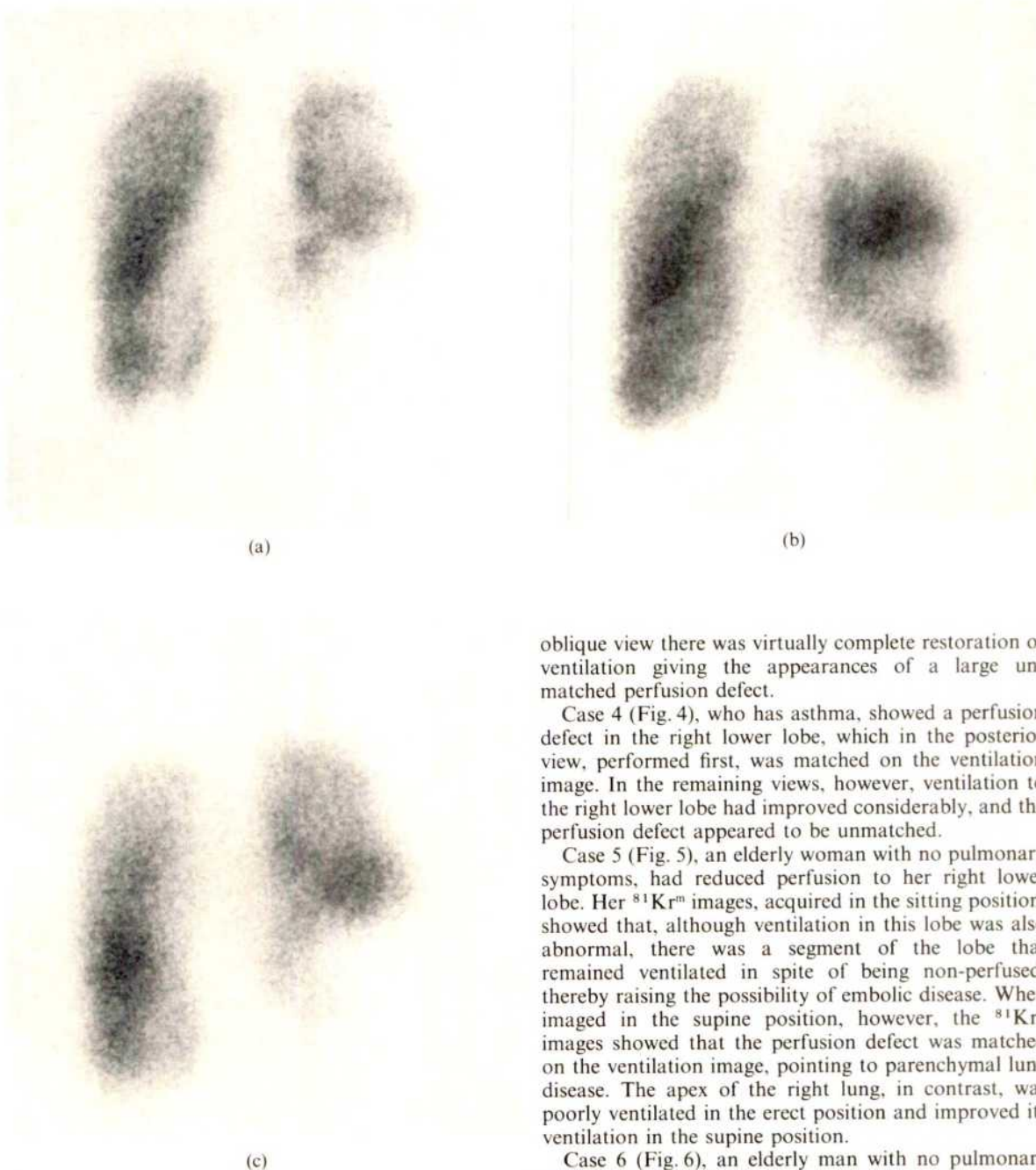


Figure 5. Case 5. (a) ^{99}Tc -MAA lung scan showing a substantial defect of perfusion in the right lower zone in the posterior projection. (b) ^{81}Kr image from the posterior projection in the erect position showing significant focus of maintained ventilation in the right lower zone and also a loss of ventilation in the right upper zone typical of so-called "reversed" mismatch. (c) ^{81}Kr image from the posterior projection in the supine position showing an abnormal distribution of ventilation with a substantial defect in the right lower zone concordant with the perfusion image.

oblique view there was virtually complete restoration of ventilation giving the appearances of a large unmatched perfusion defect.

Case 4 (Fig. 4), who has asthma, showed a perfusion defect in the right lower lobe, which in the posterior view, performed first, was matched on the ventilation image. In the remaining views, however, ventilation to the right lower lobe had improved considerably, and the perfusion defect appeared to be unmatched.

Case 5 (Fig. 5), an elderly woman with no pulmonary symptoms, had reduced perfusion to her right lower lobe. Her ^{81}Kr images, acquired in the sitting position, showed that, although ventilation in this lobe was also abnormal, there was a segment of the lobe that remained ventilated in spite of being non-perfused, thereby raising the possibility of embolic disease. When imaged in the supine position, however, the ^{81}Kr images showed that the perfusion defect was matched on the ventilation image, pointing to parenchymal lung disease. The apex of the right lung, in contrast, was poorly ventilated in the erect position and improved its ventilation in the supine position.

Case 6 (Fig. 6), an elderly man with no pulmonary symptoms, showed reduced perfusion to the right upper lobe. Erect, the ventilation images were essentially normal, suggesting pulmonary vascular disease. However, it was noted in the supine position that ventilation to the right upper lobe was impaired.

Discussion

In parenchymal or obstructive lung disease, the ventilatory abnormality is usually constant and no difficulty is experienced in interpreting the V/Q scan. In

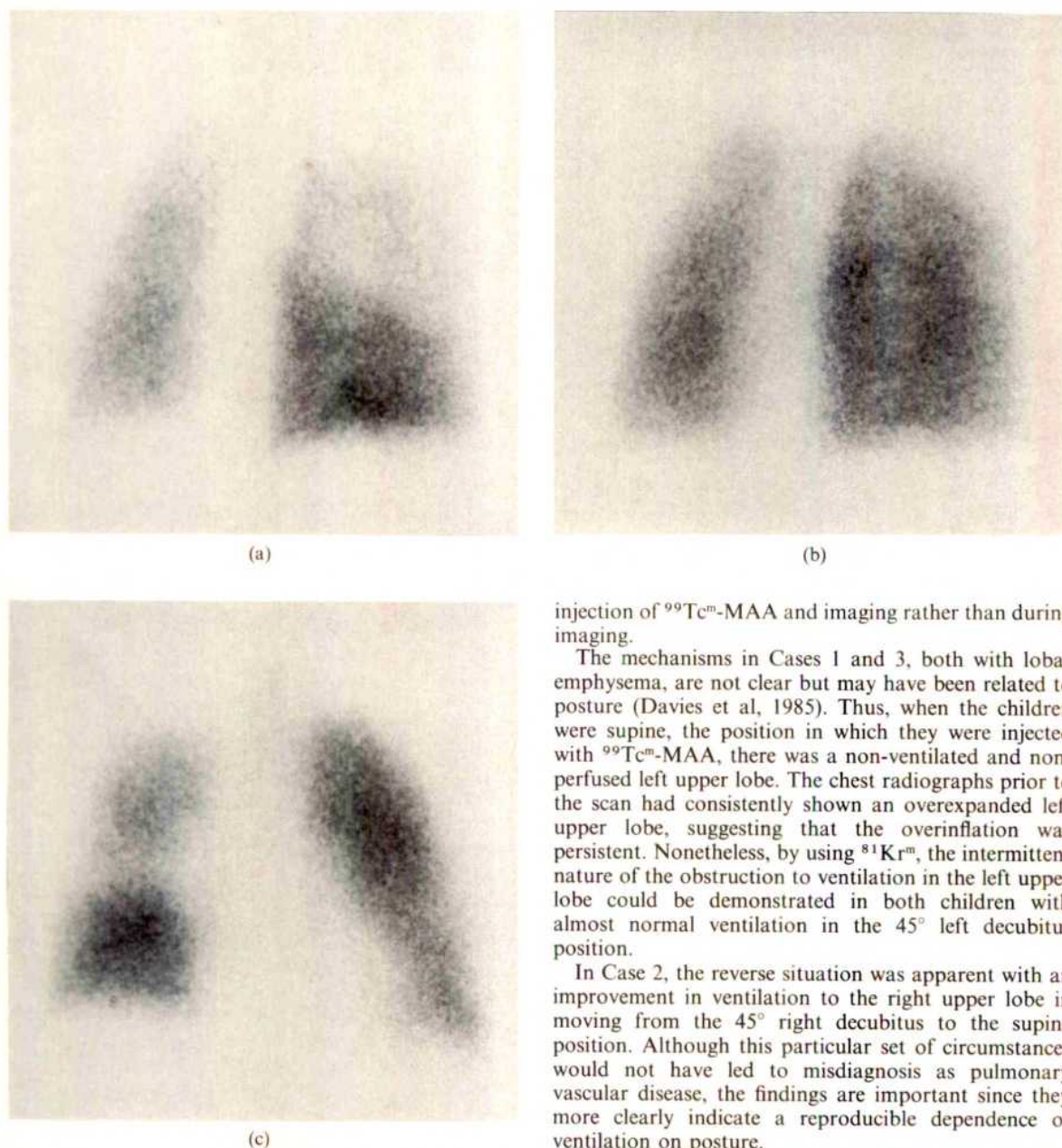


Figure 6. Case 6. (a) $^{99}\text{Tc}^{\text{m}}$ -MAA scan in the right posterior oblique projection showing substantial reduction in perfusion to the right upper lobe. (b) $^{81}\text{Kr}^{\text{m}}$ image in the right posterior oblique projection (erect position) showing normal ventilation to the right lung. (c) $^{81}\text{Kr}^{\text{m}}$ image in the supine position and anterior projection showing diminished ventilation to the right upper lobe.

this paper we present six cases in whom ventilatory abnormalities were "unstable", and which could have led to misinterpretation as pulmonary vascular disease if the changes in ventilation had occurred between

injection of $^{99}\text{Tc}^{\text{m}}$ -MAA and imaging rather than during imaging.

The mechanisms in Cases 1 and 3, both with lobar emphysema, are not clear but may have been related to posture (Davies et al, 1985). Thus, when the children were supine, the position in which they were injected with $^{99}\text{Tc}^{\text{m}}$ -MAA, there was a non-ventilated and non-perfused left upper lobe. The chest radiographs prior to the scan had consistently shown an overexpanded left upper lobe, suggesting that the overinflation was persistent. Nonetheless, by using $^{81}\text{Kr}^{\text{m}}$, the intermittent nature of the obstruction to ventilation in the left upper lobe could be demonstrated in both children with almost normal ventilation in the 45° left decubitus position.

In Case 2, the reverse situation was apparent with an improvement in ventilation to the right upper lobe in moving from the 45° right decubitus to the supine position. Although this particular set of circumstances would not have led to misdiagnosis as pulmonary vascular disease, the findings are important since they more clearly indicate a reproducible dependence of ventilation on posture.

In Case 4, an older child with asthma, the perfusion defect may have resulted from hypoxic vasoconstriction present at the time of $^{99}\text{Tc}^{\text{m}}$ -MAA injection. Although the distribution of ventilation changed, any subsequent corresponding change in perfusion would not have been recorded since the distribution of $^{99}\text{Tc}^{\text{m}}$ -MAA represents the distribution of perfusion at the time of injection. Transitory segmental or lobar ventilatory defects have been described in asthma, producing the converse situation to the above and giving rise to a so-called "reversed mismatch" (De Nardo & De Nardo, 1984). Bronchodilator aerosols, used during lung scanning of asthmatics, may be of value.

In Cases 5 and 6, the changes in ventilation to the right lung appeared to be positional. Thus in Case 5 the changes occurred in opposite directions (to apex and lower lobe) in moving from the supine to the erect position. Again, we speculate that the perfusion defect in the right lower lobe in her case was the result of hypoxic vasoconstriction in the supine position, present at the time of MAA injection. Note that in both these adults the changes in ventilation occurred in the right lung and were therefore unrelated to the possible positional effects of the enlarged heart on left lower lobe ventilation that have been recently described by Alexander et al (1988).

In parenchymal lung disease the perfusion defects usually match the ventilatory abnormalities. However, $^{99}\text{Tc}^{\text{m}}$ -MAA is usually given prior to the lung scan and it is a theoretical possibility that a lobe may be non-

ventilated and non-perfused at the time of the injection, but improve its ventilation later.

These cases document focal intermittent ventilation and suggest that a posterior ventilation view, in the same position as for the injection of $^{99}\text{Tc}^{\text{m}}$ -MAA, immediately prior to the injection may be useful.

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Magnetic resonance imaging in recurrent carcinoma of the cervix

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Abstract. Twenty patients with suspected recurrent cervical carcinoma were evaluated with computed tomography (CT) and high-field magnetic resonance imaging (MRI). Histological verification of the imaging findings were available in all cases. Computed tomography and MRI were equally effective in making the diagnosis of disease recurrence. The extent of vaginal recurrence and involvement of pelvic floor muscles was better shown on MRI than on CT.

Several studies have shown that magnetic resonance imaging (MRI) is well suited to evaluation of patients with carcinoma of the cervix (Powell et al, 1986; Togashi et al, 1986; Rubens et al, 1988; Waggenpack et al, 1988). Magnetic resonance imaging demonstrates cervical tumour as a high-intensity mass on T_2 -weighted sequences, which can readily be distinguished from normal cervical tissue. Furthermore, MRI has been shown to be accurate for detecting vaginal spread, parametrial invasion and extension to the pelvic side wall (Hricak et al, 1988).

The majority of studies reported to date have been undertaken in patients with primary carcinoma of the cervix and MRI has been assessed as a method of staging the disease. The largest series so far reported by Hricak and her colleagues (Hricak et al, 1988) in 57 patients clearly shows the advantages of MRI and discusses these with respect to the limitations of CT. However, in this study and the majority of other studies, direct comparison of the results of MRI with CT in the same patients has not been possible.

There is little information on the use of MRI for diagnosing recurrence in patients with cervical carcinoma, but in the few patients in whom the results of MRI have been reported, there is some evidence to suggest that MRI is a useful method for distinguishing recurrence from irradiation fibrosis on the basis of signal intensity on T_2 -weighted pulse sequences (Glazer et al, 1985; Ebner et al, 1988). The accuracy of CT in the detection of local recurrence is approximately 80-85% (Walsh et al, 1981; Heron et al, 1988). The main limitations of CT are the inability to differentiate fibrosis from recurrence on the basis of CT attenuation values and the inability to distinguish inflammatory change and vessels within the parametrium from tumour invasion. The diagnosis of recurrent disease therefore remains a considerable challenge and any

improvement in diagnostic information that may be achieved with MRI is to be welcomed.

The present retrospective study was carried out in 20 patients with suspected recurrence from carcinoma of the cervix to determine the value of MRI and to compare the results with those of CT.

Patients and methods

The study comprised 20 patients with a diagnosis of suspected recurrent carcinoma of the cervix in whom pathological verification of the imaging results was available. The suspicion of recurrence was based on the clinical features of pelvic pain, vaginal discharge, vaginal bleeding, lower limb swelling or a palpable mass on pelvic examination. All patients had previous, histologically proven carcinoma of the cervix (18 squamous cell, one adenocarcinoma and one anaplastic carcinoma). At primary presentation the disease had been staged clinically as Stage IB (seven patients), Stage IIA (two patients), Stage IIB (five patients), Stage IIIA (three patients) and Stage IIIB (three patients). The time between initial treatment of the primary carcinoma and the time of suspected recurrence ranged from 3 months to 14 years with a mean of 38 months. Six patients had previously undergone a total abdominal or Wertheim's hysterectomy, two had undergone a subtotal hysterectomy, two patients had an anterior exenteration and the remaining 10 patients had been treated by external-beam irradiation alone. All patients included in the study underwent pelvic CT and pelvic MRI within 2 weeks of each other.

Computed tomography was carried out at the Royal Marsden Hospital on Siemens systems (DR2 and DRH). One patient was referred from another institution following a CT examination and this was not repeated at our hospital. Computed tomography was carried out using 8 mm sections through the false pelvis at 12 or 14 mm intervals and 8 mm sections through the true pelvis at 8 or 10 mm intervals. Intravenous contrast medium was not routinely used for the initial series of

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scans but was given at the discretion of the radiologist to resolve specific problems identified on the unenhanced scans. All patients were examined with a full bladder and were prepared with oral contrast medium (sodium meglumine diatrizoate, Gastrografin 2%, Schering AG; 1000 ml given over 45 min before the examination). A vaginal tampon was inserted when possible.

Magnetic resonance imaging was performed on a Siemens Magnetom system operating at 1.5 T. Five to nine T_1 -weighted sections were obtained in the axial and sagittal planes using repetition time (TR) 0.5–0.8 s and echo time (TE) 17–30 ms with two or four acquisitions. Eleven to 15 proton density and T_2 -weighted sections were obtained with TR 2.1 s and TEs of 28 and 72 ms, respectively, with one or two acquisitions in the sagittal and axial planes. Seven-millimetre sections were used with a 3.5 mm intersection gap. Total imaging time for all four sequences with the maximum number of acquisitions and including a Scout scan amounted to approximately 70 min. Three patients were unable to complete the whole sequence of scans and in these patients, axial T_1 - and T_2 -weighted images only were available for review and comparison with CT.

At the beginning of the study, six patients were examined after the injection of 0.1 mg of intravenous Glucagon in order to reduce peristaltic artefacts. This procedure was subsequently abandoned in view of the lack of a noticeable improvement in peristaltic artefact. As with CT examinations, all patients were scanned with a full bladder and a vaginal tampon was used when possible.

The CT and MR images were each reviewed blind by two radiologists (M.P.W., J.E.H.). In the case of disagreement, a third opinion (D.B.K.) was sought and the majority view recorded.

Histological proof of the imaging diagnosis was available in all 20 patients. Histological biopsies from suspicious areas were obtained in 10 patients, hysterectomy specimens in three and an anterior exenteration specimen in one patient. Open biopsy at laparotomy was undertaken in two patients and four patients had histological proof of distant metastatic disease with no evidence of local recurrence. Distant metastases were diagnosed from ascitic fluid (one patient), liver biopsy (one patient), bronchoscopy (one patient) and in one patient distant metastases were found at post-mortem examination in the liver, lungs and stomach with no evidence of local pelvic recurrence.

Results

Of the total group of 20 patients, 14 had histological evidence of locally recurrent disease (11 central and three nodal), one of which was a large, conglomerate, pelvic side-wall mass. Four had histological evidence of distant metastases without evidence of local disease and two patients had hysterectomy specimens showing evidence of inflammatory change attributed to irradiation with no evidence of local tumour.

Table 1. Accuracy of CT and MRI in the diagnosis of central tumour recurrence

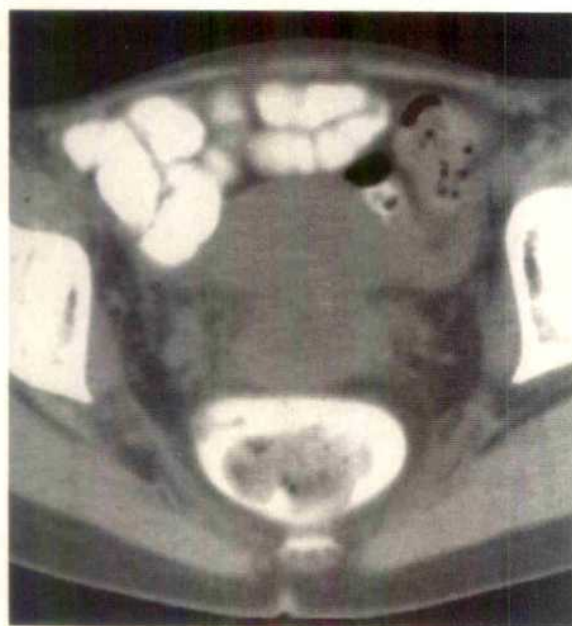
	Histology	
	Positive	Negative
CT		
Soft-tissue dense central mass	Positive 10	2
	Negative 1	7
Sensitivity 10/11 (91%)		
Specificity 7/9 (78%)		
Accuracy 17/20 (85%)		
MRI		
Central mass with high signal on T_2 -weighted images	Positive 9	2
	Negative 2	7
Sensitivity 9/11 (82%)		
Specificity 7/9 (78%)		
Accuracy 16/20 (80%)		

The accuracy of CT and MRI in the diagnosis of central tumour recurrence is shown in Table 1.

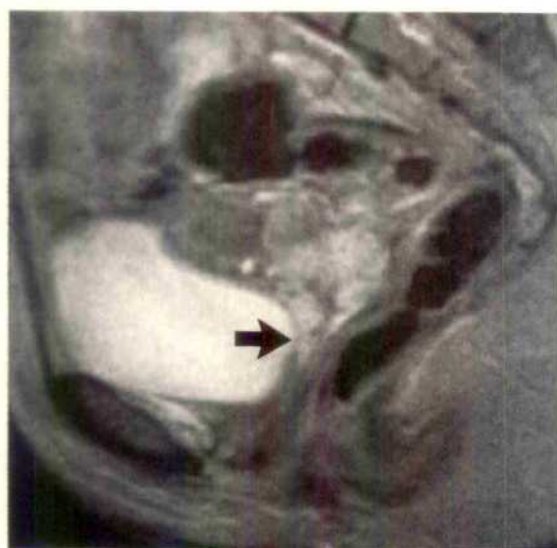
On CT a diagnosis of central recurrence was made when there was a soft-tissue dense mass present in the expected position of the cervix. The masses ranged from 3.5 to 7 cm in diameter. With MRI the central recurrences were seen as irregular masses of similar signal intensity to muscle on T_1 -weighted images. On proton density images the mass showed a slight increase in signal relative to muscle and on T_2 -weighted images, areas of high signal intensity were seen within the mass (Fig. 1).

In two patients, recurrent disease was incorrectly diagnosed on the basis of areas of increased signal intensity within the cervix on T_2 -weighted images and on the basis of a mass at the vaginal vault on CT. Both patients had been treated with external-beam irradiation within the previous 3 months. Hysterectomy was performed 1 month following CT and MR examinations. In both patients the specimen revealed inflammatory changes only within the abnormal cervix (Fig. 2).

One patient was false negative for recurrence on MRI but positive for recurrence on CT. Computed tomography showed a bulky cervix of 3.5 cm in diameter but signal intensity from the cervix on T_2 -weighted MRI did not show any areas of high signal intensity relative to muscle. At examination under anaesthesia, however, recurrent disease was noted superficially on the surface of the cervix and extending into the vaginal fornix on the left. The other patient who was false negative for recurrence on both CT and MRI had an unusual pelvic mass. On CT, this had the appearance of a thick-walled cyst and on MRI this collection showed a relatively high signal on both T_1 - and T_2 -weighted images, which was thought to indicate proteinaceous fluid, pus or altered blood. Subsequent aspiration of the collection, however, revealed malignant squamous cells diagnostic of recurrent disease.



(a)



(b)

Figure 1. (a) Axial CT section demonstrates recurrent cervical carcinoma as a 3 cm x 5 cm mass of the same density as normal uterus. Note bilateral parametrial extension. (b) Midline sagittal T_2 -weighted MR section (TR 2.1 s, TE 72 ms) shows the recurrent carcinoma as a high-signal-intensity mass easily differentiated from the anteverted uterus. The sagittal orientation enables visualization of tumour extension down the anterior vaginal wall (arrow).

The numbers of patients demonstrating additional features of recurrent disease are shown in Table II.

Lymph node enlargement was demonstrated in five patients by both CT and MRI. In three, the lymph

nodes were the only site of recurrent disease. On CT the enlarged nodes appeared as masses of uniform, soft-tissue density. With MRI the enlarged nodes showed low intensity on T_1 -weighted images, intermediate intensity relative to muscle on proton density images and high signal intensity relative to muscle on T_2 -weighted images. The single most useful MR sequence for identifying enlarged nodes was the proton density sequence. On T_1 -weighted sequences, the low intensity of nodes may lead to potential confusion between vessels and nodal enlargement and on T_2 -weighted images, high signal nodes showed little contrast with surrounding fat.

Vaginal extension of a central tumour recurrence was seen in three patients. Invasion of the pelvic side wall or pelvic floor muscles was more clearly identified with MRI than with CT, although a correct diagnosis of recurrent disease was made with both techniques in all three patients (Fig. 3a, b). Magnetic resonance imaging was particularly helpful in demonstrating the relationship of the recurrence to the urethra, as this structure is clearly demarcated on T_2 -weighted images (Fig. 4).

Bladder invasion was diagnosed in three patients on MRI and in two patients on CT. On MRI, bladder invasion was seen as an area of high signal from the bladder wall on proton density and T_2 -weighted images (Fig. 5). Involvement of the bladder wall was confirmed in two patients, but in the third patient, biopsy from an area shown to be abnormal on MRI showed bullous oedema only.

Associated findings

Uterus. Uterine abnormalities were more readily assessed with MRI than with CT. In two patients, uterine fibroids were demonstrated as rounded masses of low intensity on both T_1 - and T_2 -weighted images whereas they were not discernible on CT. In a further two patients, the uterus appeared slightly enlarged on CT but on the MR images, it was shown to be obstructed with an enlarged cavity. In one of these patients the cavity contained material of high signal intensity on both T_1 - and T_2 -weighted images and this was correctly diagnosed to represent haemorrhage within the uterine cavity. Confirmation was obtained at post-mortem examination.

Hydroureter. In three patients, unilateral hydroureter was shown by MRI and CT. In all three patients the hydroureter was caused by recurrent pelvic disease.

Lymphocoeles. Lymphocoeles were noted in the pelvis in two patients who had previously undergone hysterectomy. On CT these were readily recognized as thin-walled structures containing uniform fluid density. On MRI, lymphocoeles showed low signal intensities on T_1 -weighted images, and high signal intensity on T_2 -weighted images, typical of clear fluid.

Radiotherapy changes. Irradiation changes were noted in the pelvis in four patients. On CT these four patients showed the characteristic signs of a perirectal halo of fat and thickened utero-sacral ligaments. Computed

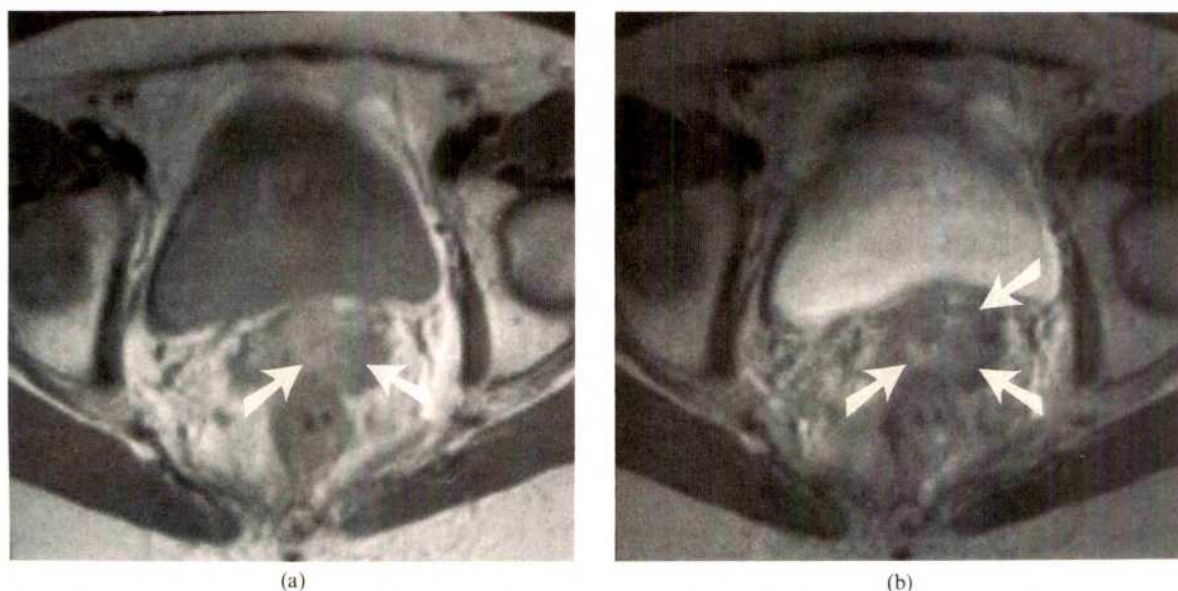


Figure 2. (a) Proton density and (b) T_2 -weighted axial images (TR 2.1 s, TE 28 and 72 ms, respectively) through the cervix show inhomogeneous areas of high signal centrally (arrowed). Hysterectomy specimen revealed no evidence of viable tumour but only inflammatory changes attributed to radiation.

tomography also showed abnormally thickened bowel wall within the irradiated fields in three patients. Although MRI also demonstrated the perirectal halo, this was not as well shown as with CT, and bowel wall thickening was more difficult to assess being clearly visible on MRI in only one patient.

Discussion

The diagnosis of recurrence of carcinoma of the cervix may be extremely difficult on clinical examination (Heron et al, 1988) and CT has been a valuable adjunct for the assessment of these patients (Vick et al, 1984). However, studies undertaken to evaluate the role of CT

in this group of patients have highlighted several limitations of the technique. The major difficulties encountered are the inability to characterize strands of tissue in parametrium that may represent tumour spread, post-irradiation fibrosis or small parametrial vessels. Furthermore, the transverse plane is not ideal for examination of the gynaecological organs and this constraint makes it difficult to detect tumour invasion of the lower uterus or upper vagina.

Magnetic resonance imaging has major advantages over CT for examination of the female pelvis. First, the gynaecological organs can be imaged in the sagittal plane, which is particularly useful for demonstrating

Table II. Additional features of recurrent disease

Feature	No. of patients		Verification/comment	
	CT	MRI		
Nodal disease (as only evidence of recurrence)	5 (3)	5 (3)	Biopsy proven	3
			Response to radiotherapy	1
			Progressive enlargement	1
Parametrial extension (to pelvic side wall)	8 (4)	8 (4)	Biopsy proven	2
			On basis of identical imaging findings	1
Vaginal extension (with pelvic side wall involvement)	2 (0)	3 (2)	Biopsy proven	2
Bladder wall involvement	2	3	Cystoscopic biopsy (1 MR false positive)	3
Bone involvement	1	2	MRI only	1
			MRI more extensive than CT	1

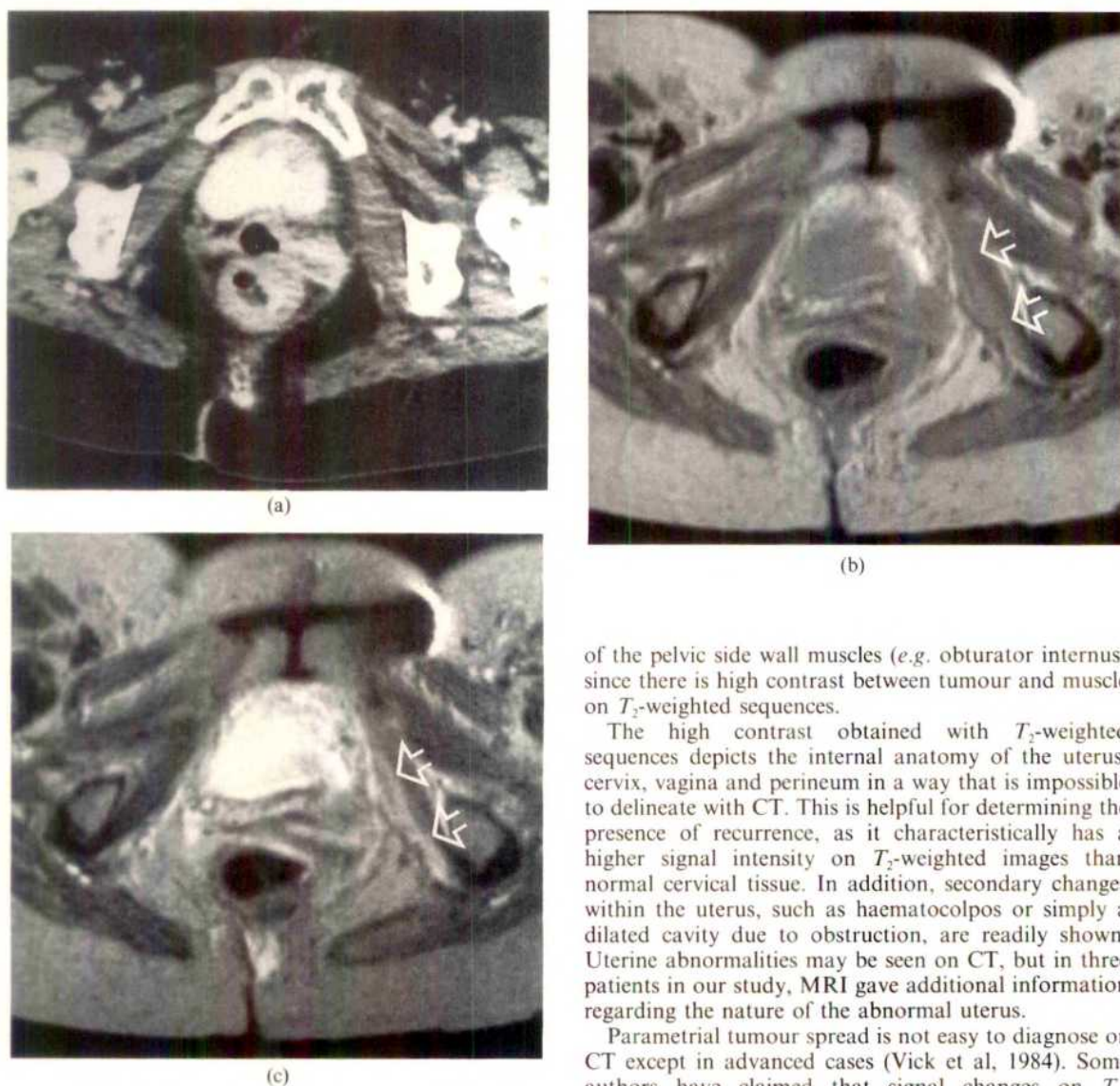


Figure 3. (a) A CT section through the pubic symphysis shows an enhancing mass of recurrent tumour abutting the left levator ani muscle. (b) Proton density and (c) T_2 -weighted MR sections (TR 2.1 s, TE 28 and 72 ms, respectively) show recurrent tumour mass involving the left side of the vagina and also demonstrate abnormal high signal in the left obturator internus muscle (arrowed). Biopsy from this muscle demonstrated tumour involvement. The signal void and artefact in the left groin on the MR images was due to a needle retained in the subcutaneous tissue.

involvement of the uterus or upper vagina. In our study, vaginal extension of tumour was readily shown by MRI in one patient where the extent of involvement on CT was less easily appreciated. Magnetic resonance imaging is particularly helpful in showing extension of tumour through the pelvic floor into the perineum and invasion

of the pelvic side wall muscles (*e.g.* obturator internus) since there is high contrast between tumour and muscle on T_2 -weighted sequences.

The high contrast obtained with T_2 -weighted sequences depicts the internal anatomy of the uterus, cervix, vagina and perineum in a way that is impossible to delineate with CT. This is helpful for determining the presence of recurrence, as it characteristically has a higher signal intensity on T_2 -weighted images than normal cervical tissue. In addition, secondary changes within the uterus, such as haematocolpos or simply a dilated cavity due to obstruction, are readily shown. Uterine abnormalities may be seen on CT, but in three patients in our study, MRI gave additional information regarding the nature of the abnormal uterus.

Parametrial tumour spread is not easy to diagnose on CT except in advanced cases (Vick et al, 1984). Some authors have claimed that signal changes on T_2 -weighted MR images may be helpful in this context (Togashi et al, 1986; Hricak et al, 1988). In our group of patients, parametrial extension was best appreciated by the morphological appearances of T_1 -weighted images and it is therefore not surprising that the results of CT and MRI are identical.

In a recent study, Ebner et al (1988) found that MRI was an accurate method of distinguishing fibrosis from recurrent tumour in six patients in whom recurrence and fibrosis co-existed. Other authors have also addressed the topic and with varying results. Thus, Bies et al (1984) investigated nine patients with suspected recurrent carcinoma of the cervix but were unable to distinguish radiation changes from recurrent tumour. Ebner et al (1988) emphasize that signal intensities from radiation damage change with time. Recent irradiation change produces high signal intensities on T_2 -weighted



Figure 4. (a) A CT section through the vagina shows a vaginal recurrence as an enhancing tumour mass whose borders are difficult to define. (b) T_2 -weighted (TR 2.1 s, TE 72 ms) MR section clearly delineates the vaginal tumour and shows its relationship to the urethra (arrow).

images whereas late fibrosis gives a low signal on T_2 -weighted images.

From the results of our study it is not possible to make conclusive statements regarding the ability of MRI to distinguish radiation fibrosis from recurrence, since only four patients showed definite evidence of radiation changes on MRI and CT. Three of these patients had extensive pelvic recurrence in association with fibrosis, and surgery was not undertaken. Confirmation of recurrence was obtained at biopsy only and histological mapping of areas of tumour and areas of fibrosis could therefore not be obtained. In the fourth patient there was no evidence of a mass in the pelvis

and, therefore, the differential diagnosis of tumour versus fibrosis was not an issue.

Inflammatory reaction within the cervix was confused with tumour recurrence on MRI and CT in two patients. Both patients had been treated with radiotherapy during the previous 3 months and it is likely that the inflammatory changes were related to irradiation. On MRI, a high signal intensity was obtained on T_2 -weighted sequences from the cervical mass in both patients. These findings are in agreement with those from Ebner et al (1988) who found that early post-irradiation change gives rise to a high signal intensity on T_2 -weighted sequences. On CT the masses

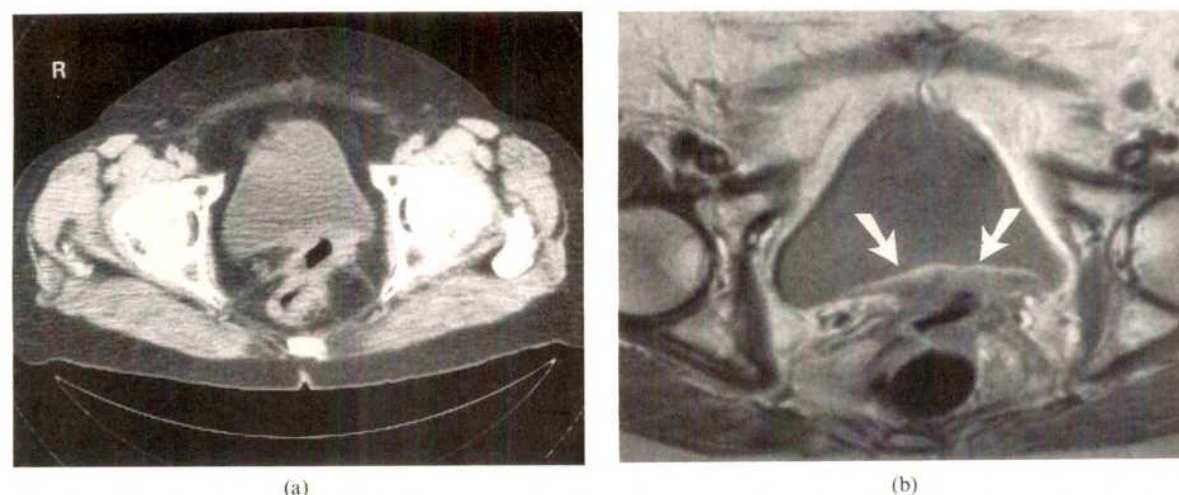


Figure 5. (a) Axial CT section demonstrates bladder wall thickening in continuity with recurrent tumour in the upper vagina. (b) A proton density (TR 2.1 s, TE 28 ms) MR section shows high signal from the area of bladder wall involved by recurrent cervical carcinoma (arrows). Note the marked chemical shift effect causing a dark line down the right side of the bladder wall and a light line down the left side of the bladder wall. These are caused by misregistration of fat and water protons in the frequency encoded (horizontal) direction.

were of uniform CT density and enlargement of the cervix was the only criterion used for diagnosing recurrence.

Lymph node metastases were identified in five patients and both techniques identified disease in the same lymph node sites. Although the numbers of patients are small, these results support those of others who consider that MRI has no distinct advantage over CT for detecting lymph node metastases (Lee et al, 1984).

Magnetic resonance imaging may be more sensitive than CT for detecting bladder wall invasion since the low intensity signal from the normal bladder wall on T_2 -weighted images is replaced by a higher intensity signal when the wall is replaced by tumour. However, oedema and inflammatory change also give rise to an increase in signal on T_2 -weighted sequences, which may lead to confusion as in one of our patients. With CT, the density of the bladder wall is unaffected by tumour, oedema or inflammation. Thus, the diagnosis of bladder wall invasion can only be made with certainty when intraluminal tumour contiguous with extraluminal disease is identified.

In the assessment of bone metastases, CT is clearly inferior to MRI. Marrow infiltration is elegantly demonstrated by MRI in many different tumours and it is now well established that MRI is likely to have an important role in the assessment of marrow disease in such conditions as myeloma and leukaemia (Daffner et al, 1986). It is not surprising, therefore, that MRI showed more extensive involvement than CT in both our patients with metastatic bone disease.

Overall, in this group of patients, CT and MRI appear to be equally accurate in the diagnosis of recurrence. Magnetic resonance imaging made a correct diagnosis of local pelvic recurrence in 12 out of 14 patients (three nodal and nine central recurrences) and CT in 13 out of 14 patients (three nodal and 10 central recurrences). In our view, MRI demonstrates lower pelvic recurrences, which may invade the pelvic floor and pelvic side walls, more elegantly than CT and frequently shows more extensive disease. This information should be helpful for determining the optimal approach to management by selecting those suitable for surgical resection more accurately than has previously been possible.

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Congenital ureteric diverticula in children and adults: classification, radiological and clinical features

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Abstract. To date, about 100 cases of a blind-ending branch of a bifid ureter have been reported. We present 13 clinically, radiologically and histologically evaluated cases of congenital ureteric diverticulum. We believe this anomaly is not as rare as hitherto believed and suggest the term congenital ureteric diverticulum for a blind-ending branch of a bifid ureter.

Ureteric diverticula were first described by Herbert in 1904 and numerous individual cases have since been described (Culp, 1947; Lenaghan, 1962; Youngen & Persky, 1965; Gettel et al, 1972; Caffey, 1978).

In 1979, Caller et al described in detail 22 cases of ureteric anomalies, studying both the clinical and pathological features and discussing normal embryonic development as well as the embryogenesis of ureteric duplication.

Embryogenesis

Embryologically, congenital ureteric anomalies are the result of irregular development of the ureteric bud before it reaches metanephrogenic tissue (Potter, 1972).

In man, the ureteric bud appears in the 4th week of embryonic life; development may cease before reaching metanephrogenic tissue, in which case it usually does not branch and ceases to grow. If this occurs there will be no differentiation of metanephrogenic tissue with resulting renal aplasia and ureteric atresia. Branching of

the ureteric ampulla during further development is always dichotomous. The two newly created branches can behave in different ways. One branch may develop regularly and reach metanephrogenic tissue to become a ureter. The other branch may develop only partially and end blindly before reaching metanephrogenic tissue. Branching may be rudimentary or non-existent and can be deformed in various ways. It may imitate the shape of the pelvis or produce a lateral ureteric branch or diverticulum.

Observations

In the past 10 years ureteric diverticula have been diagnosed in 13 patients, aged 4 to 57 years. Findings are summarized in Table I.

Ureteric diverticula are more frequent in the female (nine out of 13). In eight out of 13 cases they were on the left side.

Five cases of ureteric diverticulum were symptomless, while eight out of 13 cases were symptomatic with, for

Table I. Findings in 13 cases of congenital ureteric diverticulum

Case no.	Age (years)	Sex	Side	Clinical symptoms		Methods of diagnosis		Treatment
				Yes	No	Excretory urography	Retrograde pyelography	
1	3	F	L		—	+	+	None
2	4	F	L		—		+	Diverticulectomy
3	5	F	L	+		+		Diverticulectomy
4	6	F	L	+		+	+	Diverticulectomy
5	7	F	L	+		+		Diverticulectomy
6	42	F	R	+		+	+	Diverticulectomy
7	42	M	L	+			+	Diverticulectomy
8	45	F	L		—	+	+	None
9	47	F	R	+		+		Diverticulectomy
10	48	F	R	+		+		None
11	50	M	R		—	+		None
12	52	M	L		—	+		None
13	57	M	R	+		+		None



Figure 1. An excretory urogram revealing a ureteral diverticulum on the right side.

instance, recurrent urinary tract infection, high sedimentation rate or pyuria.

Larger, rounded diverticula were more frequently associated with urinary tract infection. Most were revealed coincidentally by uretero-ureteric reflux during excretory urography (Fig. 1).

Appearances were similar in both children and adults and diverticula could be found anywhere along the ureters from the renal pelvis to the urinary bladder; their distribution is shown in Fig. 2.

Discussion

Precise data on the frequency of ureteric anomalies are not available.

In 1947, Culp made the first systematic classification using the term "blind-ending ureter"; de Filippi et al (1977) used the term "blind ureteral buds". We would agree with the opinion of Rank et al (1960) that there is no difference between congenital ureteric diverticulum and a blind-ending or a bifid ureter, considering embryogenesis and histological structure.

Finder et al (1982) quoted less than 100 cases of blind-ending ureters described in the literature. Bizarre,

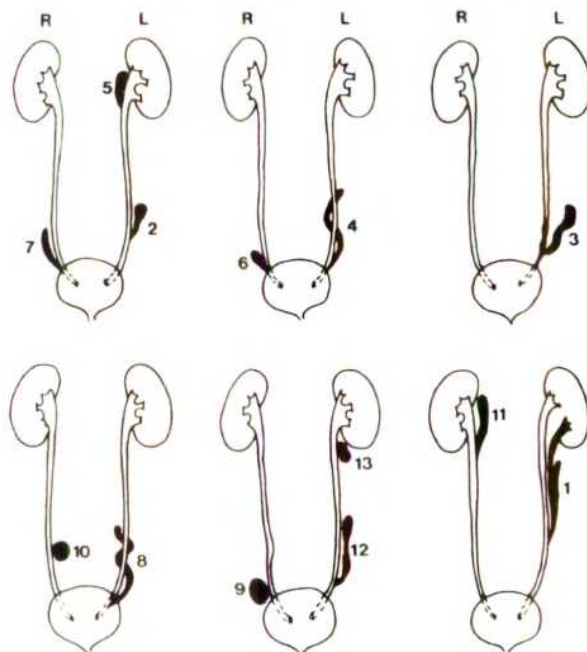


Figure 2. Diagrammatic representation of the site and shape of ureteric diverticula in our cases.

clinical manifestations have been described (Rank et al, 1960; Haber, 1973; Merimsky, 1980; Kerschot et al, 1983) ranging from pronounced clinical symptoms to accidental findings.

Considering 13 patients with ureteral diverticulum, it appears that a typical symptomatology in children and lack of clear symptoms and urinary abnormalities in adults may be responsible for missed or late diagnosis and consequently for a lower estimation of the prevalence of this anomaly in the general population. We believe many ureteric anomalies remain unidentified.

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Technical note

X-ray protection considerations for mammography screening centres

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The inception of the National Breast Screening Programme, following publication of the report (Department of Health and Social Security (DHSS), 1986) of a working group under the Chairmanship of Sir Patrick Forrest, led to the construction of a significant number of new mammography rooms including mobile units, with many more being proposed for the next few years. As a result, Radiation Protection Advisers (RPAs) are now being required to give advice on room construction for these units.

The *Guidance Notes For Health Authorities On Mammographic Equipment Requirements For Breast Cancer Screening* published by the DHSS (1987), whilst giving clear guidelines to facilitate standardization on most technical aspects of mammography screening/assessment centres, do not give any outline of the protection requirements, merely stating in paragraph 3.7.3. that "Radiation protection and operational features must meet the requirements of the local Radiation Protection Adviser." Such Radiation Protection Advisers will need access to both attenuation data and scatter measurements on which to base their recommendations. This paper presents measurements at mammographic energies of both the attenuation properties of a range of materials that could be used in barrier construction, and phantom scatter measurements. In addition, the application of these results to the situation that will be found in the new screening centres

and measurements performed to confirm the conclusions are presented.

Attenuation measurements

It is felt that lead is an inappropriate material for protection against scattered radiation from mammography, the difficulty and expense of obtaining the very thin thicknesses required being considerable. This could well lead to gross over-protection and hence unnecessary weight, a critical consideration for a mobile unit. We have determined that for a 35 kVp mammography beam the transmission through 0.2 mm sheet lead is $< 7 \times 10^{-6}$ of the incident radiation.

It was decided, therefore, to measure the broad-beam attenuation at mammography energies for a variety of different materials that might be considered suitable for these specialized situations, namely plasterboard, glass, steel, aluminium and wood. The measurements were carried out using an MDH 20X5-6M chamber, which is an ionization chamber specially designed for mammographic use and has an essentially flat response throughout the energy range of interest. The units used were a CGR Senographe 600T and a Philips Diagnost M, both with molybdenum anodes and 0.03 mm molybdenum added filtration.

The attenuation curves obtained at a machine setting of 35 kVp, under broad-beam conditions, are presented in Fig. 1 and a summary of the densities, half-value

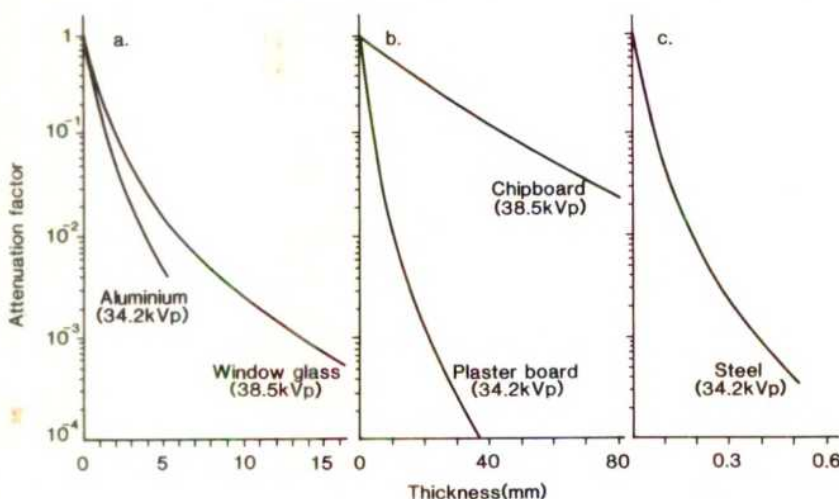


Figure 1. Attenuation measurements for some common materials suitable for secondary protective barriers at mammographic energies: (a) aluminium and window glass, (b) plasterboard and chipboard and (c) steel.

Table I. Half-value layer (HVL) and tenth-value layer (TVL) at mammographic energies for various common materials

	Density (g/cm ³)	HVL (mm)	TVL (mm)	Measured kVp
Aluminium	2.7	0.375	1.5	34.2
Steel	7.8	0.02	0.07	34.2
Plasterboard	0.85	1.3	4.2	34.2
Glass	2.48	0.5	2.2	38.5
Chipboard	0.63	12.25	45.5	38.5

layers (HVL) and tenth-value layers (TVL) is given in Table I. The composition of most of the sample materials is reasonably standard. However, the data presented for the chipboard should only be used as a rough guide for similar materials as density and composition will change from sample to sample.

Attenuation of both primary and scattered radiation was measured for aluminium and showed no significant difference. We have thus assumed that primary beam data may be used for design calculations of both primary and secondary barriers for all materials and that this will not add greatly to the amount of protection required.

Scatter ratio

For the newer mammography units, the primary beam is fully contained and effectively stopped by the cassette tray. Thus it is only necessary to consider scattered radiation for barrier calculations. The calculation of such secondary barrier requirements requires knowledge of the dose-rate due to scattered radiation from the breast.

The scatter from several different units has been measured over the past few years using a 5 cm thick breast equivalent phantom (BR12 material) and a field size larger than the 15.8 cm diameter. In all cases, measurements between 20 and 50 cm above the plane of the phantom gave the highest readings. Some of the units gave asymmetrical distributions and in all cases the scatter levels dropped off towards the back of the unit because of shielding by the unit, cassette holder attachment, etc.

Scatter around a CGR Senographe unit was measured at a setting of 35 kVp. The maximum around the unit was found to be at a height of 50 cm above the plane of the phantom, a scatter ratio being obtained at this point of

$$\frac{\text{Scatter at 1 m from phantom}}{\text{Output of tube at 1 m}} = 5 \times 10^{-4}$$

This measurement is consistent with our measurements on other units.

A search through the literature has not yielded any truly comparable data. The National Council on Radiological Protection and Measurements (NCRP) Report 49 (1976) Table B-2 gives a scatter ratio of 8×10^{-4} for 50 kVp, a tungsten anode, scattering angle 120° and field size of 400 cm^2 , and British Standards

4094 (BSI, 1971) Fig. 18c gives a scatter ratio of 1.2×10^{-4} for a 90° scattering angle, 30 kVp, tungsten anode and beam size of 100 cm^2 at the phantom. Our measurement is not inconsistent with these values.

Application to a Forrest Report Screening Unit

In order to be able to use the above data in an actual situation it is necessary to make assumptions about patient throughput, exposure factors and tube output. In addition, the design criteria must be defined. Only then is it possible to calculate barrier requirements.

Workload and output assumptions

Paragraph 8.7 of the Forrest Report (DHSS, 1986) gives an estimate of a maximum throughput of 40 women (each having two single-view mammograms) in a half-day session. Therefore, a maximum of 80 women or 160 mammograms per day has been assumed. This works out at an average of approximately 2.6 min between exposures, assuming two busy 3.5 h sessions of screening, and is unlikely to be significantly exceeded in any 8 h working period as required in calculations of time-average dose-rate.

All units are to use molybdenum tube X-ray units capable of between 20 and 40 kVp. Mammography is typically carried out at 28 kVp, possibly going up to 32 kVp for very dense large breasts. None of the centres involved in the screening programme within the North Western Regional Health Authority use higher kVp settings. We therefore chose a nominal 35 kVp for our output, scatter and attenuation measurements to give a built-in safety factor. Considering that the output at 35 kVp is roughly twice that at 28 kVp, a safety factor of a minimum of 2 is introduced.

The predominant view will be the medio-lateral oblique with some centres also doing a cranio-caudal view on each breast. In general, the oblique view requires a slightly higher mAs and the workload data presented below is based on this. Two of the screening centres recently set up in the North Western Region have regularly noted the post-exposure indication of mAs for each exposure. The data presented in Table II were obtained from 50 consecutive women radiographed in each of the centres. Both centres use the CGR Senographe 500/600 series fitted with 5:1 ratio grids, Min R screens with Ortho M film and 3.5 min processing. The exposures were made using the automatic exposure devices of the units. As can be seen,

Table II. Exposure factors for two screening centres, obtained from reviewing 50 consecutive patients having lateral oblique examinations

		mAs range	Mean mAs ($\pm$ standard deviation)
Centre 1	Screening	25–250	87 (± 63)
	Assessment	12–323	82.5 (± 71)
Centre 2	Screening	6–252	111 (± 73)

the range of mAs is wide, with an average value of around 100 mAs.

Over the past few years output measurements have been undertaken on several mammography units around the North Western Region. For a 35 kVp setting a range of 44–84 μGy per mAs at 1 m focus distance has been measured, with a mean value of 64.6 (± 13) $\mu\text{Gy mAs}^{-1}$.

Based on the above we have taken the following as our design baselines in calculating dose-rates for a Forrest Screening Centre:

Exposure factors (per film): 100 mAs at 35 kVp
 Tube output at 1 m: 70 $\mu\text{Gy mAs}^{-1}$
 Throughput in 8-h working period: 160 exposures

Design calculations

Combining the factors discussed above with the scatter factor of 5×10^{-4} , as defined earlier, yields a time-averaged dose-rate (TADR) (averaged over an 8-h working day) for scattered radiation of 70 $\mu\text{Sv h}^{-1}$ at 1 m from the patient and an instantaneous dose-rate (IDR) (averaged over 1 min) for scattered radiation of 210 $\mu\text{Sv h}^{-1}$. These are the dose-rate quantities, as defined in the *Ionizing Radiations Regulations 1985* (HMSO, 1985), needed to calculate protective barrier thicknesses.

The calculations presented here assume that the required barrier will be 1 m from the patient. This might at first seem rather near but our experience is that mammography units are often placed near to walls in very confined circumstances, and certainly vans do not allow a spacious environment. If barriers are to be further away, use of the inverse square law will be adequately accurate for reductions of the required attenuation factors.

It is our policy to calculate protection requirements so that the TADR is reduced to $< 2.5 \mu\text{Sv h}^{-1}$, provided that any likely occupancy of the surrounding areas would ensure that no member of the public would be exposed to more than 1 mSv per year as required in the National Radiological Protection Board (NRPB) publication GS4 (1986). The dose-rate criteria of $2.5 \mu\text{Sv h}^{-1}$ for designation of a supervised area is stipulated in Schedule 6 of the *Ionizing Radiations Regulations 1985* (HMSO, 1985).

The recently published *Guidance Notes for the Protection of Persons Against Ionizing Radiations Arising from Medical and Dental Use* (NRPB, 1988) has a footnote on page 9 to the effect that shielding should reduce the IDR to $< 7.5 \mu\text{Sv h}^{-1}$. It also stipulates that shielding for a control panel should reduce the TADR to $< 1 \mu\text{Sv h}^{-1}$. Results presented here will be based on all three of these design criteria, namely:

1. TADR $< 2.5 \mu\text{Sv h}^{-1}$ for the room exterior.
2. IDR $< 7.5 \mu\text{Sv h}^{-1}$ for the room exterior.
3. TADR $< 1 \mu\text{Sv h}^{-1}$ for the control area protection.

Protective barrier attenuation factors required for these design criteria, given the dose-rates calculated

Table III. Secondary barrier requirements 1 m from a mammography unit for the Forrest Report workload

Design criteria	TADR $< 2.5 \mu\text{Sv h}^{-1}$	IDR $< 7.5 \mu\text{Sv h}^{-1}$	TADR $< 1 \mu\text{Sv h}^{-1}$
Attenuation factor	0.036	0.036	0.014
Barrier thickness (mm)			
Aluminium	2.5	2.5	3.5
Steel	0.125	0.125	0.175
Plasterboard	6.8	6.8	9.3
Glass	3.6	3.6	5.2
Chipboard	70	70	99.7

above, are given in Table III. These can be translated into thicknesses of material using the attenuation data presented in Table I. It can be seen that, with the exception of chipboard, these thicknesses are easily obtained in practice. Hence, wood should not be the sole material of choice for a near barrier, but could well form part of the protection with a lining of either aluminium or steel.

Environmental confirmation

We have been able to measure scatter around two actual units being used for mammographic screening in two centres in the North Western Health Authority. These units have a reasonable throughput although not yet up to the 160 mammograms per day predicted by the Forrest Committee (DHSS, 1986).

The scatter was measured using standard film badge monitors left in position around the inside of the room walls for between 4 and 8 weeks. Three series of measurements have been performed during periods with a throughput of 463 and 300 (Centre 2) and 250 (Centre 1) patients. The effective energy obtained by analysis of the density patterns on the badges was in the range 11–19 keV and is roughly that expected from the beam qualities in use. The estimated accuracy of this technique in estimating dose is around $\pm 30\%$.

The two centres are those described in Table II. Centre 1 takes only medio-lateral oblique views, one of each breast, whereas Centre 2 presently also takes a cranio-caudal view for women between the ages of 50 and 55 years.

Analysis of the film badge readings has led to the production of the isodose curves shown in Fig. 2 for a typical workload of 160 exposures per day. Figure 2a shows the $25 \mu\text{Sv h}^{-1}$ point in a horizontal plane at approximately waist height around the unit. It combines the results of three separate measurement periods, the spread of the individual isodose curves being indicated by the shaded area. The three separate monitoring periods gave reasonably consistent results as indicated by the spread of only 30 cm maximum. Figure 2b shows the $25 \mu\text{Sv h}^{-1}$ isodose curve in a vertical plane through the cassette holder and at right angles to the midline of the unit. These data are based on only one measuring period and so no spread is shown.

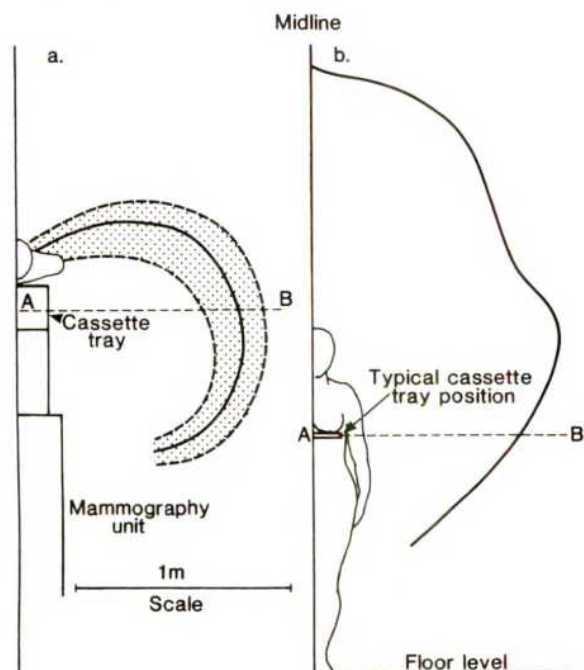


Figure 2. Plot of $25 \mu\text{Sv h}^{-1}$ isodose curves around a screening unit with a Forrest Report workload level: (a) plan section through cassette tray and (b) vertical section through cassette tray.

The maximum TADR at 1 m for the Forrest Report workload was estimated from these measurements as 30, 42 and $59 \mu\text{Sv h}^{-1}$ for each of the three sets of measurements. These figures can be compared with our estimation of $70 \mu\text{Sv h}^{-1}$ for the 35 kVp situation given earlier in this paper.

Environmental dose on both the inside and outside of the X-ray room walls of these centres has also been measured. One room was constructed of two sheets of plasterboard and the other of medium density fibreboard with 2 mm sheet aluminium applied. Dose readings of up to 3 mSv, over a 4-week monitoring period, were recorded on the inner badges but no readings $> 0.01 \text{ mSv}$ (the lower limit of sensitivity) were

recorded on the outer badges, indicating that the walls were providing adequate protection.

Discussion

Our measurements show that it is not appropriate to resort to expensive and heavy lead protection for constructional protection in mammography, even with the high throughput of the National Breast Screening Centres. Plasterboard will provide a good solution to static situations with maybe aluminium or steel sheet being used to line doors, etc. if these are close to the unit. It might well be sufficient to ensure that doors are made of solid wood and are placed at some distance from the unit.

Plasterboard is not a practical proposition in mobile units as it does not withstand the inherent mechanical vibration, and hence sheet aluminium or steel would be the materials of choice. Low windows are not usually a feature of mammography rooms, a measure of privacy being required. Obscured windows might be included and the usual thickness of glass will cope with this situation.

Acknowledgments

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Case report

Foregut cyst of the mediastinum: fluid re-accumulation after transbronchial needle aspiration

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Cysts arising from embryonic remnants of the primitive foregut include bronchogenic cyst, oesophageal duplication and neurenteric cyst (Kirwan et al, 1973). The place of computed tomography (CT) and needle biopsy in the diagnosis and the management of foregut cysts of the mediastinum has been demonstrated (Schwartz et al, 1985, 1986; Kuhlman et al, 1988).

We report a case of a foregut cyst diagnosed and treated by these methods, but without long-term symptomatic relief inasmuch as symptoms recurred 3 years later with re-accumulation of fluid.

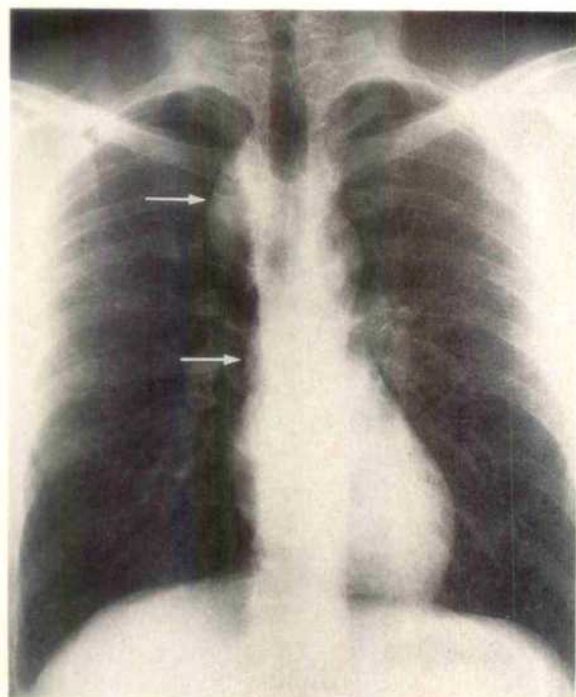
Case report

In 1986, a 27-year-old man complained of vague right thoracic pain. A right mediastinal mass was discovered on chest radiographs (Fig. 1a, b). A CT scan showed a tubular cystic mass (internal density +30 HU). This had regular and smooth

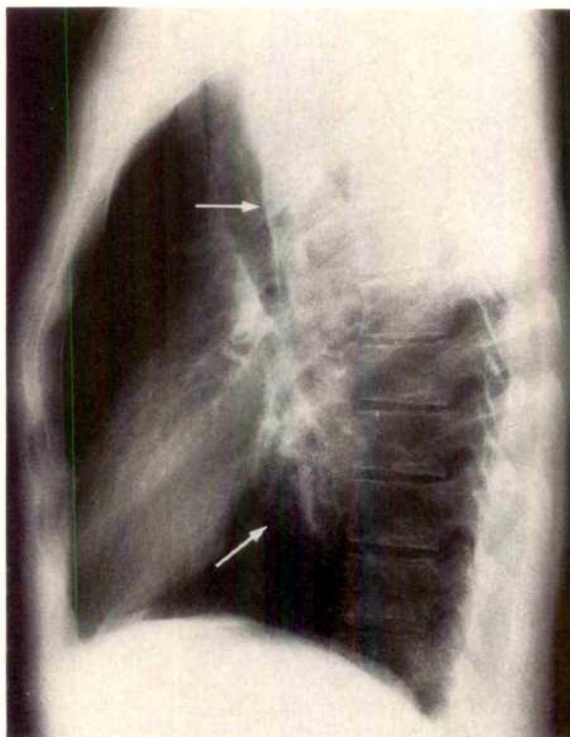
borders and was located on the right side of the entire thoracic oesophagus (Fig. 1c, d). There was no subdiaphragmatic extension and a CT scan of the upper abdomen did not show any abnormality. In particular, no pancreatic lesion was detected. A rigid bronchoscopy was performed and a Storz transbronchial needle was used to puncture the cyst transcarinally. This aspiration biopsy needle has an outer diameter of 1.4 mm. Seventy millilitres of clear, yellow fluid were aspirated and the procedure was well tolerated.

Cultures of the fluid were negative and cytological examination showed no malignant cells. The presumptive diagnosis, based on CT and needle aspiration, was oesophageal duplication cyst. A control chest radiograph following needle aspiration showed obvious regression of the mediastinal mass (Fig. 1e) and the patient was sent home without further treatment.

Follow-up chest radiographs in 1986 and 1987 demonstrated



(a)



(b)

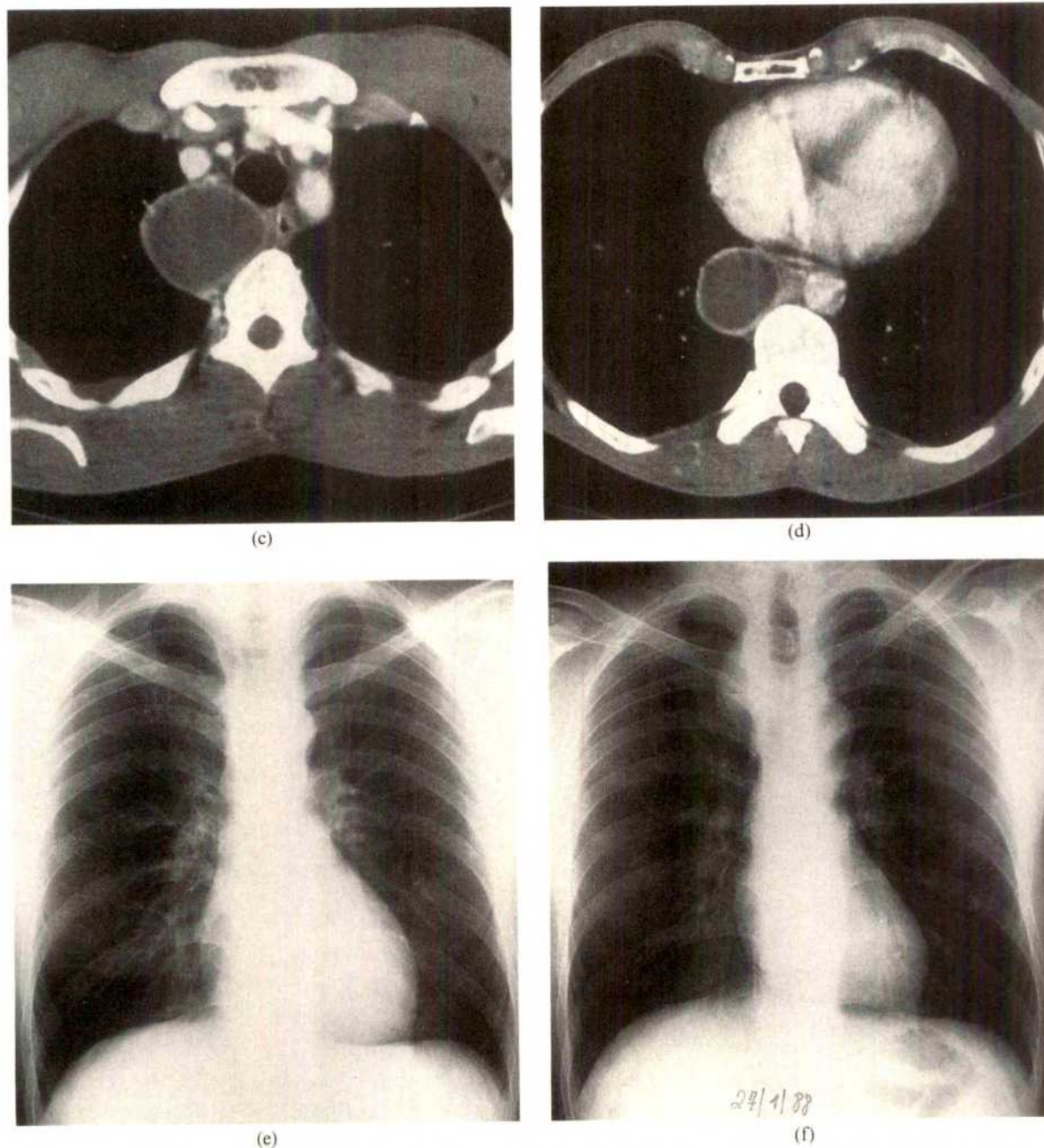


Figure 1. Initial (a) postero-anterior and (b) lateral chest radiographs showing a right mediastinal mass (arrows). (c, d) Contrast-enhanced CT scans showing a cystic mass, adjacent to the thoracic oesophagus throughout its length. (e) Chest radiograph after transbronchial needle aspiration showing regression of the cyst. (f) Chest radiograph, 2 years later. The cyst has regained its initial size from re-accumulation of fluid.

a progressive growth of the mass. In 1988, the patient was admitted again because of recurrence of thoracic pain. Chest radiographs and CT showed the mediastinal cyst had regained its initial dimensions (Fig. 1f). The internal density values remained low: from +20 to +30 HU. Scintigrams with labelled red blood cells and labelled white blood cells did not demonstrate haemorrhage or infection in the cyst. Worsening

pain prompted surgical excision with pathological confirmation of oesophageal duplication.

Discussion

The traditional approach to foregut cysts of the mediastinum, especially when symptomatic, has been

surgical excision for definitive diagnosis and treatment (Sirivella et al, 1985). Computed tomography now provides a strong presumptive diagnosis of benign cyst (Snyder et al, 1985; Fitch et al, 1986).

Differential diagnosis of cystic masses of the posterior mediastinum includes foregut cyst of the mediastinum, pancreatic pseudocyst, hydatid cyst, thoracic duct cyst, cystic lymphangioma, lymphocoele, meningocoele, loculated pleural effusion, pericardial cyst, abscess and old haematoma. In our case, the diagnosis of oesophageal duplication cyst was suggested by the close proximity of the tubular cyst to the oesophagus and by the absence of any previous medical history.

Transbronchial or transoesophageal needle aspiration has been advocated in mediastinal cysts to exclude any neoplastic or infectious element of the lesion (Schwartz et al, 1985, 1986); CT and needle aspiration may thus avoid surgery.

In a series of five benign mediastinal cysts with transbronchial or transoesophageal needle aspiration, Kuhlman et al (1988) observed a regression in the size of the cysts in each case and a disappearance of the symptoms in one symptomatic patient. The authors concluded: "Further study will be required to determine whether aspirated mediastinal cysts eventually re-accumulate fluid and whether long-term symptomatic relief can be achieved using this technique". We did observe re-accumulation of fluid in our case. Although spontaneous resolution of mediastinal cysts has been

reported (Martin et al, 1988), surgery may still be necessary for definitive treatment in symptomatic cases. The morbidity related to thoracotomy makes repeated aspiration a therapeutic alternative.

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Case of the month

Jekyll and Hyde chest radiographs

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(Received March 1988 and in revised form April 1988)

A full-term, male infant was admitted to the Special Care Baby Unit immediately following birth with cyanosis and respiratory distress. The pregnancy had been uneventful and the mother had three other children who were all well. The baby was intubated and ventilated but remained persistently hypoxic with a respiratory acidosis. The chest radiograph on admission is shown in Fig. 1.

Treatment for a presumed streptococcal pneumonia was instituted but the baby remained unwell. Over the following days an expanding "cystic area" was noted in the right lower zone (Fig. 2) and, following increasing mediastinal shift, three chest drains were inserted (Fig. 3).

What abnormalities are shown on the three chest radiographs? What is your differential diagnosis and what further investigations would you perform?

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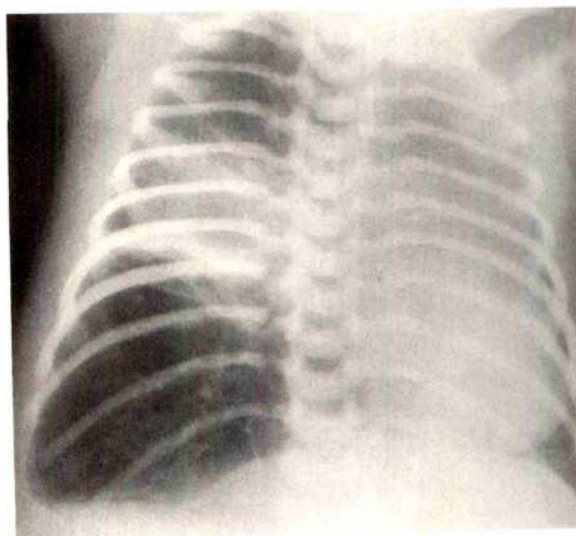


Figure 2. Chest radiograph taken after 7 days.

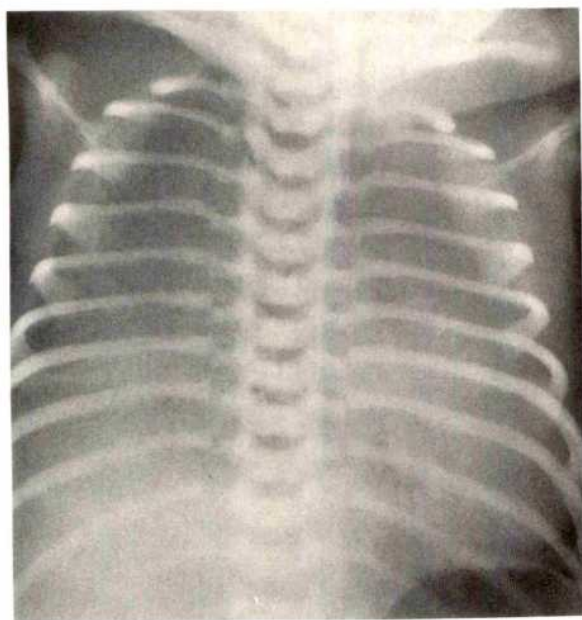


Figure 1. Chest radiograph on admission to the Special Care Baby Unit.

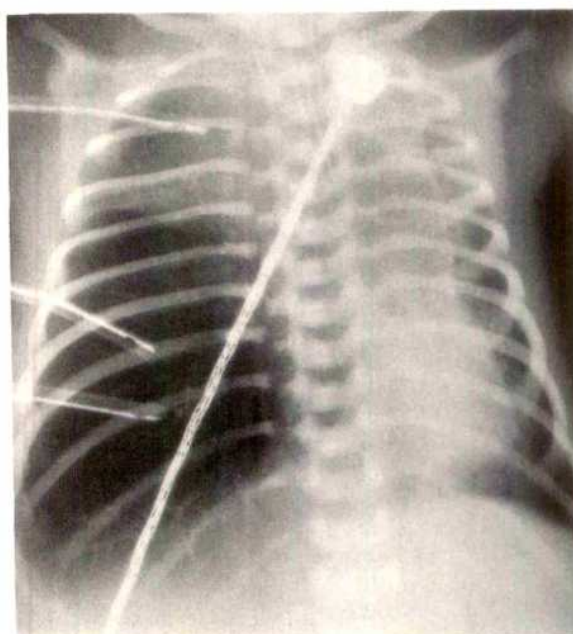


Figure 3. Chest radiograph taken on the 10th day.

On the initial chest radiograph the cardiac apex is shifted to the left as is the upper mediastinum, shown by the position of the endotracheal tube. There is diffuse shadowing throughout both lungs, compatible with retained fetal fluid, and more dense opacification of the right lower zone. The second radiograph (Fig. 2) shows marked overexpansion of the right lung, with emphysematous changes of the lower and middle lobes, and mediastinal shift to the left. This is even more severe on the third radiograph (Fig. 3) with considerable herniation of the hyperinflated right lung across the midline, inversion of the hemi-diaphragm and increased emphysematous changes in the right lower and middle lobes. The chest drain tubes were inserted on the assumption that a pneumothorax was present.

The chest radiographic appearances could be due to hyperinflation from obstruction of a bronchus. In a neonate (Caffey, 1978; Alford & Armstrong, 1986), this may be due to intrabronchial obstruction by a mucus plug, foreign body or tumour, extrinsic compression by a mediastinal mass (such as a bronchogenic cyst), or a vascular ring. Similar appearances can be produced by bronchial stenosis, congenital lobar emphysema, a congenital lung cyst or cystic adenomatoid malformation when the cystic component predominates. A tension pneumothorax should not cause confusion if a lung edge and absent vessels are observed, and in cases of difficulty a horizontal beam lateral view should be obtained. Congenital lobar emphysema presents in the neonatal period with respiratory distress due to air trapping, which results in massive emphysema, collapse of adjacent lobes and mediastinal shift. When seen on the first day of life, the affected, distended lobe may initially be fluid filled, as shown in Fig. 1. However, the upper lobes, most commonly the left, and sometimes the middle lobe, are usually involved, and only rarely the lower lobes (Cremin & Movsowitz, 1971).

The most important differential diagnosis was considered to be compression of the right main bronchus by a vascular ring. A contrast-enhanced computed tomographic scan of the mediastinum was initially performed, but due to artefacts from the endotracheal tube, failed to provide any diagnostic information. An anomalous left pulmonary artery, which arose from the right pulmonary artery and crossed to the left behind the trachea, was confirmed by cine angiography, which also showed a small patent ductus arteriosus (Fig. 4). Division of the pulmonary sling and re-implantation of the left pulmonary artery into the main pulmonary artery was performed 13 days after the child was born and at the same time the patent ductus was divided.

An anomalous left pulmonary artery usually arises from the first part of the right pulmonary artery, passes over the right main bronchus and crosses the midline between the trachea and oesophagus. This presents with



Figure 4. Pulmonary cine angiogram (frontal view with cranial tilt). The tip of the catheter lies in the main pulmonary artery. The anomalous origin of the left pulmonary artery passes over the right main bronchus and behind the trachea to reach the left hilum. The arrowhead points to the patent ductus arteriosus. The endotracheal tube is in the left main bronchus.

obstructive symptoms and signs due to compression of any of the airways with which the anomalous artery is intimately related, usually the right main bronchus, as in our patient. It can be simply differentiated from the variety of other aberrant vessels and vascular rings on a lateral barium swallow (Berdon & Baker, 1972) as it is the only vascular anomaly to pass between the trachea and oesophagus, resulting in anterior oesophageal indentation. Although this is an unusual cause of unilateral emphysema in the neonate it is important to consider it in the differential diagnosis as the surgical management is quite different from that required for congenital lobar emphysema or other causes of this appearance.

Acknowledgment

We would like to thank Dr Fleming and Mr Dhasmana for permission to report this case.

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Short communication

Upper-half body irradiation for oat cell carcinoma of the bronchus

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(Received July 1988 and in revised form January 1989)

Small-cell anaplastic carcinoma of the bronchus (SCCB) is considered to be a chemosensitive tumour. For many physicians, chemotherapy is the treatment of first choice. However, despite prolonged and aggressive therapy, overall 2-year survival of less than 10% may be expected (Spiro, 1985), which, for example, is very similar to the bad prognosis associated with high-grade cerebral gliomas (Bloom, 1982).

Radiotherapy has an established role in the palliation of advanced disease. We have previously investigated the use of single, large fractions of radiotherapy in patients with drug-resistant multiple myeloma and shown excellent responses and prolonged survival (Rostom et al, 1984). As the majority of patients present with disseminated disease, we have investigated the use of a single fraction of radiotherapy to the upper half of the body (including the liver) in 24 patients with SCCB.

Materials and methods

Twenty-four patients (11 male and 13 female) with small-cell anaplastic carcinoma of the bronchus have been treated with upper-half body irradiation (UHBI) since 1983. In 18 patients, this was the initial therapy. Five patients had relapsed following systemic chemotherapy, one of whom had also received radiotherapy to the mediastinum and neck. A further patient was treated prophylactically following lobectomy for a peripheral anaplastic small-cell carcinoma. Disease was classified as limited to one hemithorax or the ipsilateral supraclavicular fossa or as being more extensive (Table I). Of the 14 patients with extensive disease, two presented with epileptic fits but had negative radionuclide scans of the brain. A third had cerebral metastases confirmed by scanning.

Patients were treated with 8 MV photons from a linear accelerator. With the patient sitting, the upper half of the body from the vertex to below the 12th rib was treated with a parallel opposed pair of anterior and posterior fields; 8.5 Gy was prescribed at mid-thoracic separation, and 14 mm lead lung shields were used in the anterior field to reduce the uncorrected lung dose to approximately 6.4 Gy. In four patients with extensive pulmonary disease, only the unaffected lung was shielded. Eighty millimetres of thick lead shielding in the anterior beam reduced the dose to the mouth to ~4.25 Gy.

All patients were treated as inpatients and acute side-effects were minimized by pre-medication with steroids, anti-emetics, sedation and intravenous fluids.

Five patients were selected to receive mediastinal radiotherapy, 20 Gy mid-point dose in five fractions in 1 week, commencing approximately 1 month following UHBI.

Table I. Disease status of 24 patients with anaplastic carcinoma of the bronchus treated with UHBI

	Initial treatment	Treatment on relapse	Total
Limited disease	8	1	9
Extensive disease	10	4	14
Post-operative adjuvant	1	—	1
Total	19	5	24

Results

The procedure was well tolerated. The patients experienced transient nausea and vomiting, which was effectively controlled with anti-emetics, sedatives and steroids, and were discharged generally the day after treatment. All developed alopecia. The majority experienced worthwhile immediate symptomatic improvement in their condition.

The overall median survival, however, was only 3 months and was no different for limited or extensive disease (2 versus 3 months). Only one patient remains alive. She received prophylactic UHBI after a lobectomy for a peripheral carcinoma. She relapsed with bilateral ovarian metastases but remains well following oophorectomy and irradiation to the lower half of the body. Only two other patients survived for more than 1 year (12 and 13 months).

The five patients who had received prior chemotherapy did particularly badly, all dying within 4 months of UHBI. Their survival from commencement of chemotherapy ranged from 4 to 14 months (median 10 months).

One patient achieved a complete response to UBHI alone. She had limited disease but relapsed after 8 months on the anterior chest wall and subsequently in the mediastinum. Five patients received mediastinal radiotherapy 1 month following UHBI without survival benefit. Four patients had symptomatic relapse outside the treatment field. One patient with brain metastases at presentation survived for 13 months; however, all patients with cerebral metastases ultimately relapsed in this site and at least two further patients presented in relapse with epileptic fits.

Discussion

Despite prolonged and aggressive chemotherapy, less than 10% of patients with SCCB can expect to be alive 2 years after diagnosis. Many of those fortunate enough to become long-term survivors will still relapse and die from their disease or suffer severe neurological impairment (Spiro, 1985). We have

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consequently explored alternative methods of treating this common malignancy.

We have investigated the use of single, large fractions of radiotherapy in patients with drug-resistant multiple myeloma and shown excellent response and prolonged survival. Acute reactions were limited and well tolerated (Rostom et al, 1984). Patients were admitted to hospital overnight and the majority were discharged the next day.

Oat cell carcinoma is particularly radiosensitive and early studies of radical local treatment in patients with "operable" disease indicated that in a small proportion, long-term survival was possible (Miller et al, 1969). Urtasun et al (1982) explored sequential upper- and lower-half body radiotherapy with a mediastinal boost in SCCB in an attempt to control both local disease and systemic metastases. Early results suggested that, at least for localized disease, survival was equivalent to that achieved with chemotherapy. Using a similar protocol, Eichhorn et al (1983) showed a 100% complete response rate and good local control confirmed at autopsy, but a high initial death rate from pneumonitis.

As the majority of patients relapse in the chest, liver or brain, we chose to irradiate the upper half of the body, including the liver. Only four patients relapsed outside the treatment field. No cases of radiation pneumonitis have been seen with our technique of partial lung shielding.

Our results have been disappointing, although, as has been confirmed by others, the majority of patients had prompt symptomatic improvement (Salazar et al, 1986). Only one patient achieved a complete response to treatment and the median survival of 3 months was particularly poor. The addition of a mediastinal boost had no effect on survival and although on occasion UHBI provided effective palliation in patients with liver or cerebral metastases, it was not effective in preventing relapse in these sites. We believe that UHBI should

be restricted to patients with uncontrolled pain for whom it may provide very effective palliation, and to selected patients unfit for chemotherapy.

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Films, screens and cassettes for mammography

THE EDITOR—SIR,

In a recent paper on films, screens and cassettes for mammography (Law & Kirkpatrick, 1989) we included results from certain products of 3M and Dupont. After that paper was prepared we learnt that the 3M film "SX315" was a pre-production sample of their FM film and we inserted a footnote to that effect. Such samples may not represent the final product. We were later told by 3M that the sample of MS film that they supplied to us previously was below normal standard. They then gave us fresh boxes of MS and of FM film.

At the same time, and quite coincidentally, Dupont sent us a box of their new Microvision film, which we understand differs from the three Dupont films referred to in our paper. This letter reports our results from all three films.

The X-ray set and processor used in our paper were no longer available for this work, and the present results were obtained on a CGR 600t X-ray set and a Dupont T5A processor using Kodak chemicals. The MinR film-screen combination showed a score on this system that was only 0.5 higher than on the previous one.

The image score results are shown in Table I, and are compared with the previous results from our paper. Relative

speeds are given in Table II and are also compared with our previous results. For the Dupont film, comparison is made with the mean results for the three films seen previously, which differed very little among themselves. Among the 3M products, the choice of film-screen combinations tried was according to the manufacturers suggestions.

All three new films show some improvement in image score. The greatest improvement is shown by the MS film, and with MinR screens this performed as well as MinR-MinR but at virtually the same dose. The FM film has improved by a smaller amount, and its performance remains very mediocre in image score. In our view this cannot outweigh its low dose.

The new Dupont film gives results that are quite good but that are matched or exceeded by several other combinations, often at very similar doses. A fuller report on those results is contained in a paper submitted for publication.

Yours, etc.,

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(Received January 1989)

Table I. Image scores from radiographs of a "Barts" phantom

Film	Screen	Image score now	Image score previously
Cronex microvision	MinR	54.3 ± 0.7	52.4 ± 0.6 ^a
	Cronex ortho micro	54.8 ± 0.7	51.7 ± 0.9 ^a
3M MS	Min R	55.0 ± 0.9	52.5 ± 0.8
	Trimax T ₁	55.7 ± 0.6	52.3 ± 1.0
3M FM	Min R	51.1 ± 0.7	49.6 ± 0.5
	Trimax T ₂	50.0 ± 0.7	48.1 ± 0.6

^aMean of three different Cronex films.

Table II. Relative doses for unit density in radiographs of a "Barts" phantom (1.0 for MinR-MinR)

Film	Screen	Relative dose now	Relative dose previously
Cronex microvision	MinR	0.44	0.45 ^a
	Cronex ortho micro	0.41	0.43 ^a
3M MS	MinR	0.62	0.5
	Trimax T ₁	1.04	0.7
3M FM	MinR	0.25	0.25
	Trimax T ₂	0.25	0.2

^aMean of three different Cronex films.

Reference

LAW, J. & KIRKPATRICK, A. E., 1989. Films, screens and cassettes for mammography. *British Journal of Radiology*, 62, 163-167.

Biological equivalence between fractionated radiotherapy treatments

THE EDITOR—SIR,

Deehan and O'Donoghue addressed the question of generally equivalent treatments for all biological end-points in their recent short communication (Deehan & O'Donoghue, 1988). They apparently came to the conclusion that the linear-quadratic model can satisfy this, and, given that two conditions are met, it is possible to calculate an alternative to a standard treatment regime having equivalent biological effects for all tissues, without any prior knowledge of α/β ratios. It is our opinion, however, that a misleading impression is created, in that although the worked examples demonstrate the method, it is difficult to envisage the clinical usefulness of the results. Is it likely that a clinician, having prescribed a course of treatment will wish either to lengthen the overall treatment time for the same biological effect or to change the biological effect itself? It is more probable that the practical consideration will be how to decrease the number of fractions and conserve the prescribed biological effect.

Let us suppose that a uniform schedule of n fractions each of dose d , has been prescribed. After completion of n_1 fractions, can the schedule be completed in a specified number of fractions k and still retain biological equivalence? We are now looking for general equivalence between a homogeneous regime ($n - n_1$), d , and a heterogeneous regime of k fractions.

Letting $n - n_1 = n_r$ we can write generally:

$$n_r d_r = \sum_{i=1}^{i=k} d_i$$

$$n_r d_r^2 = \sum_{i=1}^{i=k} d_i^2$$

and defining a mean of the sum

$$d_m = \frac{\sum_{i=1}^{i=k} d_i}{k}$$

and a mean of the sum of squares

$$\Delta_m = \frac{\sum_{i=1}^{i=k} d_i^2}{k}$$

we can write

$$n_r = k \times \frac{d_m^2}{\Delta_m}$$

It is always the case that the square of the mean of a set of numbers is less than the mean of the squares of the same set of numbers, and hence n_r is always less than k . Hence follows an important conclusion, that the *status quo* of biological effects on all tissues cannot be re-established by a heterogeneous schedule with a number of fractions less than the number of fractions still to be given in a homogeneous schedule that has already been started.

Yours, etc.,
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(Author's reply)

THE EDITOR—SIR,

Mills and Martin-Shaw draw attention to a feature of the equations for general equivalence of fractionated radiation schedules (Equations 9 and 10, Deehan & Donoghue, 1988), which is implicit in the equations themselves and evident in the worked examples, although it is not explicitly stated in the

paper. This is, that given a uniform schedule and a heterogeneous schedule that are generally equivalent, *i.e.* independent of α/β ratios, the heterogeneous schedule must have a greater total number of fractions.

Mills and Martin-Smith suggest that it would be practically advantageous to decrease the number of fractions in a schedule and at the same time conserve the prescribed biological effect. Unfortunately, this is impossible on the basis of the linear-quadratic (LQ) model and apparently not achievable clinically (Singh, 1978). Reducing the number of fractions has the consequence of increasing the relative severity of late effects in comparison with acute effects. An example of the sort of clinical situation we were contemplating would be one where a treatment schedule has been prescribed, but for some reason the initial part was given at some other fraction size (*e.g.* an overdose). In these circumstances the use of the general equivalence equations may suggest a way in which the net biological effects of the prescribed schedule could be regained, *i.e.* the re-establishment of the biological *status quo*. We agree with Mills and Martin-Smith that it is unlikely that anyone would wish to increase the overall treatment time in an attempt to produce the same biological effects. This is because, in reality, the biological effects would not be the same. In particular, the net effect on a proliferating tumour cell population would be less. However, in the case described above it may not be necessary to increase the overall time if some portion of the "correction" schedule were given as multiple fractions per day with a suitable gap of at least 6 h between fractions.

Yours, etc.,
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Book reviews

Diagnosis and Management of Metastatic Bone Disease: a Multidisciplinary Approach. Ed. by Franklin H. Sim, pp. xix + 372, 1988 (Raven Press, New York), \$106.50. ISBN 0-88167-336-6

Although skeletal metastases occur much more frequently than primary malignant tumours of bone, very little has been written about the former, in comparison with the latter. This book makes a welcome contribution to the literature on skeletal metastases.

The book consists of 42 chapters divided into five sections: Pathogenesis, Pathophysiology and Pathology; Diagnosis; General Aspects of Treatment; Orthopaedic and Surgical Management; and Management of Specific Tumours Metastatic to Bone. As with many multi-author books, the chapters vary considerably: some are excellent, whereas others are brief and superficial, and there is some repetition.

There is much useful and detailed information in this book, but virtually no mention is made of spinal stabilization for spinal instability in the absence of spinal cord, or cauda equina compression, nor the importance of stabilizing all the lesions in a bone with a pathological fracture, to obviate the risk of a subsequent pathological fracture adjacent to an implant. The principle of relief of pain from skeletal metastases that "the dose and frequency required is that which controls the pain", is not mentioned, nor is the recent work which suggests that APD may be useful in the treatment of lytic metastases, although its use in the treatment of hypercalcaemia is referred to.

The book is well illustrated and the illustrations are well produced. Unfortunately, Figs 27.5A and B have been printed upside down.

Despite these criticisms, Dr Sim can be pleased with the book, and in particular with his own chapters. The book will make a useful contribution to our understanding and management of skeletal metastases.

C. S. B. GALASKO

An Atlas of Normal Developmental Roentgen Anatomy. 2nd edn. By Theodore E. Keats and Thomas H. Smith, pp. xii + 708, 1988 (Year Book Medical Publishers, Chicago), £104.00. ISBN 0-8151-5045-8

This atlas, the senior author of which is well renowned for other texts on normal variants and radiological measurement, sets out to demonstrate the normal radiological appearances at all ages from birth to 20 years. Separate standards for male and female are shown at each age — every 3 months for the first 2 years and then each year. The authors emphasize that the appearances are the average for each age and should not be used to assess bone age in the case of skeletal radiographs, nor do they cover the same ground as the authors' other work on normal variants. There is a useful introduction showing the techniques used for assessing skeletal maturity, with line drawings of the appearances at each age and advice on what parts of the skeleton can be usefully radiographed at each age to assess maturity. The chapters on appearances at each age start with a summary of the cardinal features seen in the skeleton, plain abdominal radiographs, barium studies of the gastrointestinal tract, urinary tract contrast studies and biliary tract studies. The illustrations are of a high quality in the main, but certain radiographs are missing at various ages due to lack of availability.

Because the difference in appearance between male and female in the gastrointestinal tract, gallbladder and upper

urinary tract in particular, is small there is a great deal of repetition, which makes for a very large text of over 700 pages and thus very expensive.

Because the text neither shows normal variants nor can be used to assess maturity accurately, this reviewer feels it will be of limited value to the person for whom it is primarily intended, that is the radiologist with limited paediatric experience. The authors' other publication on normal variants that may simulate disease is much more valuable, and this latest text adds very little of importance to the information already available.

D. W. PILLING

Clinical Imaging: An Introduction to the Role of Imaging in Clinical Practice. By Matthew Freedman, pp. xiv + 620, 1988 (Churchill Livingstone, New York), £30.00. ISBN 0-443-08623-0

This is a fairly large, much illustrated book designed for medical students doing clinical clerkships or a month's radiology course. Its express aim is "an appropriate clinical approach to diagnostic imaging", and the volume is also meant for housemen. The work integrates the different imaging modes, and is organized into seven parts, mainly by anatomy, though Part 7 is entitled "Controlling the Cost of Health Care".

The text of each chapter includes a formal pattern of "key concepts and objectives, keynotes, review questions, and a vocabulary list". This may sound prim, but turns out to be a lively and entertaining format. The book is quite excellent, and almost everything it says about sensible practice will be close to the hearts of radiologists; "if only the houseman had read this" might be the best compliment paid to it in a heated moment.

One can quibble of course. The style may be close to tugging at sleeves (p. 60): "'Doc, is it cancer?' What do you do now? You can tell him: 'May be, but it may be an old scar,' and that's why you need the old films. But he can't remember any. So what do you do? There are many situations in which people have chest radiographs but don't remember them. How many situations can you think of? ..."

Or you may disagree with some of the content. The tentative routine for a 54-year-old patient with a positive faecal blood test, normal colonic and upper GI tract endoscopy and double-contrast studies is (p. 349): "repeat double-contrast upper GI tract series at 3, 6 and 12 months, then repeat endoscopy at 12 months, and then an upper GI tract series annually for 3 years. The colon should be re-evaluated with both methods at 1 year and then followed every 2 years with both methods."

Two Canadian medical students used the text during their elective in our department, and enjoyed it. They praised it as easygoing, easily read and well organized. "The last chapter on controlling cost is very pertinent ... it provides an overview of current practice systems ... especially useful for North American students" (Regina Becker). "In these days of outrageously priced medical texts, *Clinical Imaging* is quite a good buy at £30 (Victoria Crosbie).

I agree with their praise. And the economic discussion is certainly of interest in Britain where the future of health care is under debate. This is a carefully thought-out volume, to be recommended.

THOMAS SHERWOOD

An Atlas of Radiological Interpretation: The Bones. By John Calder and Gwen Chessell, pp. 287, 1988 (Wolfe Medical, London), £20.00.
ISBN 0-7234-0953-6

As indicated in the title, this is an atlas consisting of plain radiographs paired with explanatory line diagrams. The first third of the book is on normal skeletal anatomy and bone trauma. The remainder covers bone radiology in a conventional manner, with chapters on infection, joint diseases, bone tumours, etc.

The publishers specialize in medical atlases, but, as in other books on their lists, the quality of reproduction of the radiographs is disappointing, being inversely proportional to the quality of the line diagrams and clinical illustrations. This is unfortunate as the success of an atlas of this nature largely depends on the clarity of the radiographs. These deficiencies are partially offset by the excellent adjoining line diagrams. In some cases, however, such as in osteochondritis dissecans, identification of the radiographic signs is difficult even in hindsight. Some improvement in the radiographs might have been possible by expanding the figures to include only the region of interest. Why, for example, is it necessary to reproduce a whole chest X-ray in miniature when the only salient feature is a solitary stress fracture of the first rib?

The authors have targeted the atlas at medical undergraduates and postgraduates studying for the DMRD examination. This is a difficult task as the levels of radiological knowledge of the two groups, at least in theory, should be very different. For example, anterior dislocation of the shoulder is illustrated but not posterior. Medical students should be able to recognize the former but the latter, albeit rarer, proves a greater diagnostic problem and therefore appears commonly in postgraduate vivas.

The text, by necessity in an atlas, is brief, and generally helpful, although I disagree with the statement that an osteosarcoma "arising in the cortex, is sometimes known as parosteal sarcoma". The authors have been largely successful in demonstrating the spectrum of pathology that may affect the skeleton but there are some obvious omissions like the absence of chondrosarcoma in the chapter on bone tumours.

Definitely on the plus side for this book is its modest price. Radiologists, immediately post-primary FRCR, when they are trying to assimilate a large amount of radiological knowledge, will find this atlas helpful but are unlikely to refer to it repeatedly.

A. M. DAVIES

Basics of Chest Film Interpretation. By Cynthia B. Umali, pp. xii + 148, 1988 (Little, Brown & Co, Boston), £19.50.
ISBN 0-316-88739-0

The author's intention is to provide physicians with a step-by-step guide to radiograph analysis. This is attempted by advising the reader to evaluate seven aspects of the chest radiograph. These are lung aeration, the parenchyma, vascular structures, the trachea and mediastinum, the pleura, the position of tubes and catheters and finally the soft tissues, bony structures and upper abdomen.

The text is liberally illustrated — I counted 227 figures in the 148 pages — so much so that there is not much room for text. Herein lie some shortcomings of this book, which comes across as more of a short atlas punctuated by brief notes, rather than as an adequate primer. The quality of the illustrations is variable, and the choice of some cases is curious. For instance, Fig. 2.31 shows what is meant to be a typically lobulated malignant mass. However, to my eye, and to some of my

colleagues' eyes, it is reminiscent of an arteriovenous malformation.

The text is not well balanced. Almost one-quarter of the brief discussion on the heart is about situs! We are told to ask if the patient is cyanotic or acyanotic, but there is no indication of how this information might help. How many newcomers to the chest radiograph will know what a "juxtaphrenic peak" is? This term appears three times in the text but no description or explanation is given. In general the text is like a set of lecture notes — much of the advice is sound but the presentation is more appropriate to revision than learning.

You get what you pay for and this book is inexpensive. Sadly I am unable to recommend it.

M. RUBENS

Diagnostic Picture Tests in Injury in Sport. By J. G. P. Williams, pp. 128, 1988 (Wolfe Medical Publications, London), £6.50.
ISBN 0-7234-0928-5

This pocket quiz book is based on a combination of clinical photographs and radiographs of soft tissue and bony injuries related to sporting activities. Some examples of other conditions presenting after, but not due to, injury are included. The diagnosis, together with other comments related to management and complications, is provided at the rear of the text. Of the 200 cases shown, 87 are purely radiological. The quality of the colour prints and of most of the radiographs is good. The soft-tissue detail, however, is not adequate in a few of the latter; for example in the lateral projection of the knee diagnosed as Osgood Schlatter's disease. The following comments are confined to the radiological cases.

The book is written by, and aimed at, the clinician. It was important, therefore, that the author should have been aware of the need for adequate and appropriate radiological examinations and to have pointed out any pitfalls in reaching the diagnosis. Some of the differential diagnoses offered for a radiological appearance are in fact clinical and not radiological, e.g. the differential diagnosis given for a pubic ramus stress fracture is osteitis pubis, adductor origin strain and obturator hernia.

A single AP projection of both elbows exposed simultaneously is not sufficient to determine radial head impingement on the ulna.

An os trigonum is projected over, but not fused to, the calcaneus as stated on the lateral projection of the ankle with the foot plantar flexed. Explanation is needed as to how "a positive tilt deformity characterized by an increased femoral head ratio" can be deduced from a single line drawn along the femoral neck. Some of the distortion must surely be related to the external rotation of the femoral head.

Some of the reputed avulsion and stress injuries in the growing skeleton could equally reflect normal ossification centres, particularly around the knee: the "avulsed ischial apophysis" would be more convincing if both sides had been included. Whereas the importance of the os trigonum is discussed, an os supranaviculare is considered to be an avulsion fracture of the navicular. The use of technetium diphosphonate bone scanning would have been more worthy of mention in the context of the painful normal variant than in diagnosing ankylosing spondylitis and chronic osteomyelitis, which are usually apparent on the plain radiographs.

Appropriate examples of wrist and ankle arthrograms are included. The use of knee arthrography in diagnosing loose bodies should not be encouraged, but, rather, plain radiographs with an inter-condylar view followed by

arthroscopy. Lastly, there are a few radiographs which are inappropriate for their diagnosis. The hip labelled Perthes' disease is far from typical and is most probably an adult femoral head avascular necrosis. The cause for the severely osteoarthritic shoulder is obscure, but it is not a typical "hatchet" deformity seen in recurrent dislocation of the humeral head. The appearance of the lateral femoral condyle in an intercondylar view of a child's knee is more compatible with the normal ossification pattern than with osteochondritis dissecans.

With a population becoming increasingly health-conscious and pursuing more vigorous leisure activities, both clinician and radiologist need to be educated in this expanding field. For a book of this type, however, to be of real help and not misleading to these readers, there must be an adequate input from a radiologist experienced in diagnosing skeletal problems. This has not been obtained, and consequently there are many errors in the choice of radiographs, their interpretation and subsequent discussion. For these reasons this book cannot be recommended.

N. A. BARRINGTON

Diagnostic Picture Tests in Orthopaedics. By Lipmann Kessel and Uta F. Boundy, pp. 128, 1988 (Wolfe Medical, London), £6.50.

ISBN 0-7234-0900-5

This book consists of a series of clinical photographs and radiographs illustrating a wide variety of orthopaedic conditions. The book is set out in the form of questions and answers, one or more questions being posed after each clinical photograph, radiograph, or paired clinical photograph and radiograph. The answers are given at the back of the book.

The book is aimed to stimulate interest in orthopaedics both at undergraduate and postgraduate level, as well as in general practice. As such, it is successful, and can also be used by both undergraduates and postgraduates in preparation for examinations. The book is well laid out and the quality of the illustrations is excellent. At £6.50 the book is good value and is a useful self-assessment guide to help students of whatever seniority improve their clinical diagnostic knowledge. It is recommended.

C. S. B. GALASKO

Radiological Casebook: 75 Cases with Clinico-radiological Discussion. By N. Perry and A. Chauhan, pp. xiv + 161, 1988 (Wright, London), £13.95.

ISBN 0-7236-0868-7

The aim of this book is simple: to aid candidates preparing for the final fellowship examination of the Royal College of Radiologists. In particular, it is designed to simulate the format of the radiograph viewing session. To succeed in this aim any book must fulfil several requirements. A wide range of subjects should be covered, extending from the common to the rare, using different imaging techniques. It should contain high-quality reproductions or the reader will rapidly become dispirited, blaming, perhaps justifiably, his diagnostic failure on inadequate images rather than inadequate knowledge. It should give a diagnosis, or differential, where appropriate, and discuss how this has been reached, with supporting references.

I am pleased to say that this book succeeds admirably. The cases are well laid out. The images are generally of high quality, with only one or two exceptions (in particular, the magnetic resonance images do not reflect current standards). The discussion is didactic with much useful information. Inevitably, with this style, there are statements which one could question, for example: "patients with stage I to III [Hodgkin's] disease

... should undergo staging laparotomy". It does, however, enable a large amount of information to be imparted in a readily assimilated form. A particularly pleasing feature is the use of references which are contemporary or refer to definitive studies. The majority are in readily accessible journals, thus encouraging further reading, particularly about less common conditions.

Overall, I think this is an excellent book at a readily affordable price. I would recommend it to all candidates for the fellowship examination. More experienced radiologists will also find it an absorbing test of their knowledge and observation.

P. M. TAYLOR

Clinical Radiology for Medical Students, 2nd edn. By K. T. Evans, I. H. Gravelle, G. M. Roberts and C. Hayward, pp. x + 140, 1987 (Butterworths, London), £9.95.
ISBN 0-407-01621-X

The first edition of this reasonably priced book on radiology for medical students was published in 1982, and was successful in spite of the considerable competition from other books aimed at the same section of the market. The format chosen was one with many reproductions of radiographs, many tables listing varying causes of radiographic appearances, relatively little text, and notes in heavy type emphasizing important points in the wide margin at the side of the text.

The second edition differs very little from the first. The cover is now blue instead of brown, but the book is of exactly the same length. One of the authors has been replaced, by Dr Christine Hayward. The introduction no longer talks about the 10-day rule, but mentions the potential risks of radiation. All the CT scans except one have been replaced by images from newer scanners; the majority of the ultrasound examples are unchanged, and one ultrasound of a pericardial effusion replaces a poor example of the size of an effusion shown by contrast medium in the atrium. The radiographs otherwise are almost unchanged, and one sagittal section of a head shown by MRI and three radiopharmaceutical images have been added, together with a short paragraph on digital subtraction imaging. The tables also are unchanged, except that "ileus" is now called "non-mechanical" obstruction. The pagination has been changed, with the result that one of the notes, on p. 53, refers to the cases "listed opposite", when it should refer to "over the page".

I am sorry that the different imaging techniques are not better integrated. The prime example of this is with the images of gall stones — radiographs of calculi appear in the chapter on the abdomen which is otherwise concerned with plain radiographs, whilst ultrasound of the gallbladder comes into the alimentary and biliary tract section, and in neither is there any guidance on which technique to select in particular circumstances. Similarly, the skull and spine section mentions the importance of CT in head injuries, but the relevant illustration comes much later, in the nervous system. Although there are two radiographs of non-accidental injury, there is no mention of this in the index, nor of battered babies, and this is the sort of problem where newly qualified housemen may need guidance. A few of the tables are tediously long and could be broken up into smaller tables with advantage — for instance, that on conditions characterized by loss of bone density runs to over four pages. I was also a little disappointed that there is no mention of any interventional aspect in radiology.

These criticisms are relatively trivial. The format is obviously a successful one, and the book is to be highly commended to medical students, who should be able to buy their own copies at this price, as well as finding copies in all libraries to which they have access.

W. D. JEANS

Aids to Part I FRCR. By V. P. L. Hornsby and R. K. Winter, pp. vii + 132, 1988 (Churchill Livingstone, London), £7.95. ISBN 0-443-03326-9

As the authors state, without pretension, this small book is simply a crammer for the primary examination of the FRCR. It is difficult to assess this sort of book, not only because it is aimed at a specific and ephemeral audience, but also because it gives a personal selection of those parts of the syllabus which the authors consider to be either particularly important or difficult to remember. These inclusions need not, of course, coincide with the needs of the potential user. Most readers would be looking for an *aide mémoire* which covers key issues amongst all the information they have to assimilate during 9 months. There is always the danger, of course, that the less perceptive candidate may put an appropriate reliance on such a book.

Many important points, supplemented by helpful line drawings, are included, while other topics which one would consider relevant have inevitably been missed out. The user is unlikely to find sufficient detail to answer comprehensively specific questions in the examination, including the MCQ paper. This book can only be judged by those for whom it is aimed and, even then, only on a personal basis.

G. H. WHITEHOUSE

MCQs on Diagnostic Imaging. By J. E. Dacie, pp. xi + 348, 1988 (Churchill Livingstone, London), £14.95. ISBN 0-443-03075-8

This book is a collection of 500 independent true/false type multiple-choice questions, each of five parts. The questions are arranged into sections, each covering one major body system or clinical specialty. The questions are similar in style to those used in the FRCR Part II examination, concentrating largely on the interpretation of radiological procedures but also including some relating to techniques and others on relevant clinical aspects of disease.

Each group of questions is laid out on the left-hand pages of the book, with the corresponding answers, each accompanied by a brief explanatory note, on the right-hand pages. The author has clearly paid close attention to the wording of the question stems, and I could find only a very few "leading" questions or ambiguities.

In the examination context (and this book is clearly aimed at examination candidates), varying the level of difficulty of the questions should improve discrimination between different candidates. I did get the impression that in general the questions on ultrasound, CT and particularly nuclear medicine were set at a much more basic level than those on radiographic interpretation and technique; it was not clear whether this was deliberate policy by the author or merely a reflection of the source material.

One of the major difficulties facing those who wish to write MCQs is that in real life biological variables are almost always continuous whereas the format of the MCQ requires a dichotomous type of response. The problem of translating real life "relatives" into the "absolutes" of the MCQ format will be familiar both to authors and to examination candidates. To the extent that this difficulty arises from uncertainties about the "truths" which we accept in everyday working practice, the author has neatly side-stepped this problem by deriving all her questions from a single source — Grainger and Allison's *Textbook of Diagnostic Radiology and Imaging*. Each of the MCQ answers is linked by a chapter reference to the source text. This approach virtually eliminates one of the areas of doubt about most MCQs — that is, whether the question is genuinely representative of the real-life source material. The penalty of using the single source is that no matter how

comprehensive it is, there are bound to be gaps and areas of controversy within it.

In summary, this is an excellent selection of carefully thought-out questions with annotated answers, covering the whole spectrum of radiology and imaging. Examination candidates will find it very helpful, particularly as a companion to the major textbook which provides the source of all the questions.

P. J. ROBINSON

Computing for Clinicians. By Tim Chard, pp. viii + 136, 1988 (Elmore-Chard, London), £18.00. ISBN 0-9512981-0-0

The book is a densely written essay concerning the application of computers in all fields of medical interest. It is an attempt to cover the field in as wide and useful a way as possible. Diagrams are used, where appropriate. The book does not claim to contain all the pertinent facts and excessive detail is restricted so that the book remains portable and less likely to be rendered obsolete by developments at the advancing fringe of particular specialties.

Although the author is a practising obstetrician, radiologists will find Chapter 3, dealing with the use of computers in administration, particularly useful and relevant.

The chapter on clinical data collection is of less direct relevance but contains many points and practical examples from the author's experience, which would be valuable to a radiologist considering the installation of computer systems in his/her department.

The treatment of the technical aspects of computers as parts of medical equipment is less satisfactory. The level of discussion is below that expected of FRCR candidates. For example: the author confuses the definition of the projection of a three-dimensional object in plain X-ray images with the cross-section produced by tomographic methods. Those who are primarily interested in imaging and have access to the radiological journals will find a dictionary of computing terms more useful. Four of the eight directly radiological references come from the *Clinics of North America*, vol. 24.

The book is not written to be a reference manual but the density of the text demands that it will have to be read several times before all its useful information is appreciated.

Although the author aims to serve the needs of newcomers to computing, beginners will find that the lack of a glossary is a drawback. To give due credit, there is no term which is undefined and the reader can be assured that any unusual words not defined somewhere in the text will have a meaning close to current English usage. Later editions will need to change the order of presentation. Although hardware aspects are discussed in earlier chapters, one has to wait until Chapter 5 before there is any discussion of screen displays and ergonomic factors. The best encouragement to newcomers is contained in the paragraph entitled "Teaching computers to medical students" (page 118).

The book would appeal to those radiologist managers who are about to install computer systems within their departments and radiologists who are interested in the computer developments of their clinical colleagues.

I. D. MADDISON

A Colour Atlas of Human Anatomy, 2nd edn. By R. M. H. McMinn and R. T. Hutchings, pp. 358, 1988 (Wolfe Medical Publications, London), £29.50. ISBN 0-7234-1526-9

The main subject-matter of the second edition of this atlas, as of the first, is the excellent series of colour photographs of the

skeleton and of very fine prosecutions of all parts of the human body. These are labelled in great detail and accompanied by explanatory notes, and supplemented by photographs illustrating surface anatomy, resin casts of vascular and bronchial trees and other structures, selected radiographs of good quality, and in this edition for the first time, computed tomographic (CT) and magnetic resonance imaging (MRI) scans. Coverage is extremely thorough, and it would be difficult to better the atlas as an exposition of dissecting room anatomy.

As such it is primarily directed at students of anatomy at both undergraduate and primary FRCS level (particularly the latter, and especially in countries and places where access to a dissecting room is difficult). The sales of the first edition, running to over 600 000 copies, prove without doubt that such students find it useful. The new edition is better than the old; the authors have kept note of any comments and criticisms received, and these have been incorporated in the text. The status of the principal author, as Professor of Anatomy at the Royal College of Surgeons, guarantees the accuracy of the work, and its editorial standard is beyond criticism. The labelling is excellent, and the only real problem is some loss of natural colour due to fixation; one might wish that a few pictures of fresh post-mortem specimens had been included to show the great colour difference between fresh and fixed material.

There is not much cross-sectional material, but this is not the purpose of this particular atlas; several good cross-sectional atlases already exist, and the CT and MRI scans cover this area.

The book is very good value for money if the number and quality of the colour illustrations are taken into account, and can safely be recommended to any student of anatomy.

E. H. R. FORD

Clinical Cardiac Imaging. By D. Douglas Miller, pp. xx + 684, 1988 (McGraw-Hill, New York). ISBN 0-07-042143-9

Great developments have occurred in cardiac imaging with the advent of the new imaging techniques. In keeping with this, the editors state in the preface that their "major educational goal was the creation of a text that would serve as a bridge between the basic imaging scientists and clinicians". The editor and his three associate editors are cardiologists who, it would appear, also have a major interest in nuclear medicine. This would account for the strong nuclear medicine bias seen throughout this book. The 46 other contributors are predominantly cardiologists, which reflects the limited role radiologists now have in cardiac imaging. The term cardiac imaging as opposed to cardiac radiology is appropriate in more than one way.

Part One which comprises over one-third of the text, describes non-invasive methods. Six of the 12 chapters cover radio-nuclear techniques in much detail and together they form a very up-to-date and comprehensive account of cardiac nuclear medicine that will more than satisfy most cardiologists. There is one chapter on nuclear magnetic resonance (NMR) imaging but this concentrates on the physics and other technical aspects; the chapter on NMR spectroscopy also lacks any clinical perspective.

The ultrasound section includes a chapter on two-dimensional echocardiography and one on Doppler echocardiography. There is only a very brief account of the principles, imaging views, techniques and the equipment involved in two-dimensional echo with no guidance on practical ultrasound technique. There is a reasonable account of Doppler echocardiography but, rather surprisingly, no real

mention of the role of colour Doppler. There are good but brief accounts on digital subtraction angiography and cine computed tomography (CT) but nothing on cine angiography, the major imaging method in coronary artery disease. Techniques for measuring left ventricular ejection fraction and the quantitative assessment of coronary stenosis are described but the use of digital angiography in coronary angioplasty and the problems of archiving the large amounts of data in digital cardiac studies are not covered. Even though the chest radiograph is assuming less importance in cardiology and particularly in coronary artery disease, it is rather surprising that it is totally omitted. If you do look hard in this book there are a few chest radiographs in a tidy chapter on acquired disease of the thoracic aorta (written by radiologists!).

Part Two looks at the clinical applications of cardiac imaging with sections on coronary artery disease, vascular and myocardial disease, congenital heart disease, the great vessels and cardiac surgery. The greatest part of this clinical section deals with coronary artery disease. It considers assessment of myocardial ischaemia as well as infarction and again there is a major nuclear medicine emphasis and there is much overlap between this and the sections on non-invasive methods.

Chapters on the functional significance of coronary artery stenoses and non-invasive imaging of coronary arteries with NMR, CT and ultrasound are interesting even if they have made little impact on clinical practice.

The section on congenital heart disease forms only a very small part of this textbook. There is a good account of two-dimensional echo including Doppler, more nuclear medicine and only a very brief chapter on NMR. Finally there are chapters on acquired diseases of the thoracic aorta, the pulmonary arteries and right ventricular outflow tract, non-invasive assessment versus cardiac catheterization for pre-operative evaluation of valvular heart disease and the serial evaluation of the post-operative patient.

The text is well laid out and contains many figures and illustrations that are clearly annotated; the quality of the reproductions is excellent.

I think this book is likely to be of much more interest to adult cardiologists than to radiologists. The major emphasis is on function rather than on morphology. The strong emphasis on nuclear medicine techniques is of course consistent with this approach. Cardiologists I think would find it useful but I think it is of very limited value to radiologists unless they are searching for a more detailed account of clinical nuclear cardiology. I do not think this is a balanced account of cardiac imaging for radiologists and it is not one that they are likely to consult to expand their knowledge pre-FRCR or subsequently.

J. F. REIDY

An Atlas of Clinical Nuclear Medicine. By I. Fogelman and M. Maisey, pp. x + 950, 1988 (Martin Dunitz, London), £115.00. ISBN 0-948269-34-0

A number of atlases of nuclear medicine have been published over the years. This large volume not only brings the field up to date but also provides a concise practical guide to the performance and interpretation of the wide range of studies encountered in routine nuclear medicine practice. The book is divided into eight sections, covering bone, thyroid, brain, liver and spleen, lungs, cardiac studies, and a miscellaneous group covering most of the less commonly performed radionuclide investigations. Each section begins with a brief introduction to the techniques involved and their physiological basis, followed by normal examples, the range of indications for the studies and examples of most of the common pathology encountered.

The illustrations are generally of superb quality with brief accompanying text drawing attention to the salient features. The lessons to be learned from most cases are summarized in pithy "teaching points". In attempting to be comprehensive and systematic the layout becomes a little confusing at times and there is some inevitable repetition such as when bone metastases appear first under types of pathology encountered in bone scanning, again under the investigation of bone pain and again under investigation of malignancy. A summary of the contents of each section would have been helpful to the reader finding his way around. Although there is a full index to all the conditions described, this will not be much help to a reader who has encountered unusual scintigraphic appearances and wishes to compare them with an example in the atlas. Some sort of cross-reference system to the types of abnormality illustrated would be a valuable addition to the next edition. Arrows and illustrative line drawings are used to great effect in some sections but could have been more widely employed in some scans to draw attention to relatively subtle features. However, these are relatively minor criticisms and the overall quality of the information presented is first class. The bone, thyroid, renal and cardiac chapters are of particularly high standard. The space devoted to liver and brain studies is perhaps out of proportion to their current importance.

Inevitably in a work of this size there will be some errors that have slipped past the proof reader and even some cases where the reviewer will disagree with the authors' interpretation! Figs 5.14 and 8.138 have suffered right/left inversion, in Fig. 5.143 (c) and (d) the spleen has been cut off the images altogether. Fig. 6.35 is an aerosol not krypton study (there is swallowed activity in the stomach) and there is absent ventilation to the right middle as well as lower lobe suggesting obstruction of the intermediate bronchus; Fig. 1.83 would appear to be an underexposed version of 1.82 rather than a different case, Fig. 1.23 is surely much more typical of metabolic bone disease than a malignant superscan and the patient in Fig. 1.200 has an exceptionally high vesico-ureteric junction!

This is far more than a superb coffee table book. The authors have distilled their extensive experience in a readable and accessible form. I would strongly recommend it for radiology and nuclear medicine trainees, and all practitioners of radionuclide imaging will find much to stimulate their practice and to provide a useful source of reference. It is not cheap but the price is not exorbitant bearing in mind the quality of the illustrations, many of them in colour, and of the volume as a whole.

E. P. WRIGHT

Diagnostic Imaging of the Nose and Paranasal Sinuses. By Glyn A. S. Lloyd, pp. x + 17, 1988 (Springer-Verlag, London), £66.00.

ISBN 3-540-19518-1 (Berlin)

0-387-19518-1 (New York)

Glyn Lloyd was on the staff of the Royal National Throat, Nose and Ear Hospital in Gray's Inn Road, London, from 1967 to 1988, and in this time has published numerous papers and taught innumerable registrars, both surgical and radiological. He has always been in the forefront in applying new techniques in his chosen field and the book exemplifies this attitude.

It commences with plain radiography of the sinuses and then proceeds to special techniques—conventional and computed tomography (CT), and magnetic resonance imaging (MRI). The author considers that no other investigations are now necessary, apart from the rare use of angiography before embolization.

The chapters progress through congenital disease to trauma, inflammatory disease and the other diseases affecting the region. Each is a scholarly account of the relevant literature and the radiology of each condition is discussed and illustrated by plain radiographs, CT and MRI scans, all of excellent quality. The text is written in the author's usual clear style and references are given at the end of each chapter.

It is hard to fault such a book. Few in this country have access to MRI scans and not as many to CT as should have. I suspect that these illustrations will convince those without CT scanners that the technique is an essential part of radiology and should be available in every district hospital. The only large omission is a discussion of the appearances following surgery and radiotherapy and of the difficulties encountered in assessing whether recurrence of tumour is present. A smaller omission is the absence of any guidance to the learner about when to take minor mucosal changes seriously—a more common problem for most of us than mycotic disease, giant cell lesions of the sinuses or pneumosinus dilatans, to give only three of the unusual conditions covered in the book, which each occupy much the same space as acute, chronic and allergic sinusitis together.

This book is to be very highly recommended to everyone dealing with ear, nose and throat (ENT) disease, and the publishers and author are to be congratulated on the way they have produced what will become a classic text. We now need a comprehensive book on ENT radiology—perhaps the author will have the time to write one for us.

W. D. JEANS

The British Journal of Radiology

Review article

Percutaneous interventional urology

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In the recent past, intervention in the urinary tract was the sole domain of the urological surgeon or the general surgeon with an interest in urology. With the advance of radiologically-guided interventional techniques, the approach is now multidisciplinary, involving surgeons, radiologists and pathologists. Some traditional methods of treating common urological complaints are now defunct. The implications of this are profound. They include shorter hospital inpatient stays, less use of general anaesthesia, easier planned patient management and, above all, decreased cost of patient treatment. Both patient morbidity and mortality have been reduced and, on the whole, the procedures are more acceptable.

Technology is advancing rapidly and newly acquired skills are often rather short-lived as primary therapeutic tools. For instance, extracorporeal lithotripters have reduced the demand for percutaneous nephrolithotomy, but such skills must still be practised and perfected for the treatment of complications and because not all patients are suitable.

This review concentrates on percutaneous renal work (Table I) and stresses current concepts. Specific interventional procedures are not described in detail.

Equipment requirements

Many interventional procedures, *e.g.* antegrade pyelography, can be performed on fluoroscopy units readily available in all X-ray departments. Ideally, a dedicated interventional suite is needed to satisfy both urologist and radiologist. The interventional room itself needs to be serviced by a recovery area and a nursing station where sterile trolleys can be prepared. Radiological requirements include a floating and tilting table with facilities for lithotomy procedures, and an undercouch 'C' arm with a movable intensifier with spot-film facilities. The whole unit must be impervious to irrigation fluids. High-quality, real-time ultrasound must also be easily available, ideally with ceiling-mounted, retractable probes. Piped anaesthetic gases are

needed in both the recovery area and interventional room.

The radiation dose received by the patient during percutaneous procedures is minimal, being slightly less than that for an excretory urogram (EU) (Rao *et al.*, 1987). For the operator, the dose depends upon the number of procedures performed. If the number is less than five a week, the dosage is minimal, but above this the operator may come under the category of a classified radiation worker as defined by the *Ionizing Radiations Regulations* (HMSO, 1985). The upper limit for radiologists is considered to be 20 cases a week. Recent recommendations require a dosimeter to be worn both under the lead apron, with one or more additional dosimeters on unprotected parts of the body where higher doses can be expected (BIR Radiation Protection Committee, 1987). Specifically, the radiologist's fingers are at risk. Lead glasses and a thyroid shield are other considerations.

There are many commercially available "kits" for interventional procedures. In theory, they contain all that is necessary, but in practice, there is often equipment surplus to requirements and therefore an unnecessary expense and they tend not to cater for complicated procedures. The equipment suited to individual radiologists for all interventional techniques can be purchased separately, which eliminates wastage.

Relevant anatomy, patient positioning and preparation

The kidneys lie in the perirenal space, bounded by Gerota's fascia, which also contains the proximal ureter, adrenal gland, renal artery and vein. To gain access percutaneously to the kidney, the posterior pararenal space is breached. This space contains no organs and the fat within it is continuous with the peritoneal fat line (Meyers, 1974). The anterior pararenal space lies between Gerota's fascia and the posterior parietal peritoneum. This space should not be transgressed during uncomplicated interventional procedures. These spaces communicate within the pelvis providing a route for the dissemination of infection, both as a result of pre-existing disease and intervention.

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Table I. Classification of percutaneous procedures

1. Diagnostic
 - A. Antegrade pyelography
 - B. Upper tract urodynamics (Whitaker test)
 - C. Percutaneous pyeloscopy
 - D. Renal biopsy
2. Therapeutic
 - A. Percutaneous nephrostomy
 - B. Percutaneous nephrolithotomy
 - C. Stent insertion and balloon dilatation
 - D. Percutaneous pyeloscopy, tumour ablation and pyelolysis
3. Diagnostic and therapeutic
 - A. Renal cyst puncture

The main danger of interventional procedures is vascular damage. The ideal approach should be via the lower pole of the kidney, the calyces of which are subcostal in the vast majority of cases (Wickham & Miller, 1983). Also, there is a relatively avascular line (Brodel's line), which lies 1 cm posterior to the lateral aspect of the kidney (Graves, 1954). To puncture a calyx through this line carries the least risk of vascular injury. To achieve this, interventional procedures directed at the collecting system should be performed with the patient in a 30° prone-oblique position, the kidney under investigation uppermost.

The only relative contraindication to any interventional procedure is a bleeding diathesis. Consent must be obtained after adequate explanation and appropriate pre-medication prescribed. Prophylactic parenteral antibiotic cover is essential. The choice of antibiotic depends on whether an organism has already been isolated from the urinary tract.

Antegrade pyelography

Antegrade pyelography was the first interventional technique performed (Wickham, 1954). The procedure has become safe with the introduction of the 22-gauge flexible needle, which considerably reduces damage to the renal cortex during the normal respiratory excursion of the kidney. The needles come in two lengths, 15 and 9 cm, the latter being a spinal needle. Irrespective of the indication for the study (Table II), the collecting system must be localized. There is no indication for needling the retroperitoneum blind in the hope of hitting the

Table II. Indications for antegrade pyelography

1. To identify site and cause of obstruction*
2. To identify site and cause of upper tract fistulae and leaks*
3. To measure upper tract pressures at rest and during perfusion
4. To obtain upper tract urine for bacteriology, cytology and biochemistry
5. To opacify the collecting system prior to other interventional procedures (e.g. stent insertion)*

*Where other less invasive techniques have failed.

collecting system. Guidance is best achieved using ultrasound. Modern real-time machines have excellent spatial resolution and some have purpose-made guidance attachments, although these tend to be cumbersome and maintenance of sterility can be difficult. In practice, the degree of dilatation of the collecting system determines how ultrasound should be used. The position of very dilated collecting systems can be marked on the skin and note taken of the degree of any cranial, caudal or oblique tilt. Minimally or undilated systems have to be punctured under continuous ultrasound guidance.

The main indication for antegrade studies is to define the level and cause of an obstructing upper tract lesion that has not been defined by other less invasive procedures. Such lesions are either luminal (Fig. 1), mural (Fig. 2) or extraluminal (Fig. 3). Antegrade studies will confidently differentiate between them. Once the collecting system has been punctured, a few millilitres of urine are aspirated for bacteriology. If the urine is obviously infected, the upper tract has to be drained by percutaneous nephrostomy (PCN) before antegrade studies, to avoid the danger of dissemination into the pararenal spaces and the vascular compartment. If the urine is clear, contrast medium is instilled and appropriate radiographs taken. Overdistension causes pain and extravasation and must be avoided. Significant complications are rare.

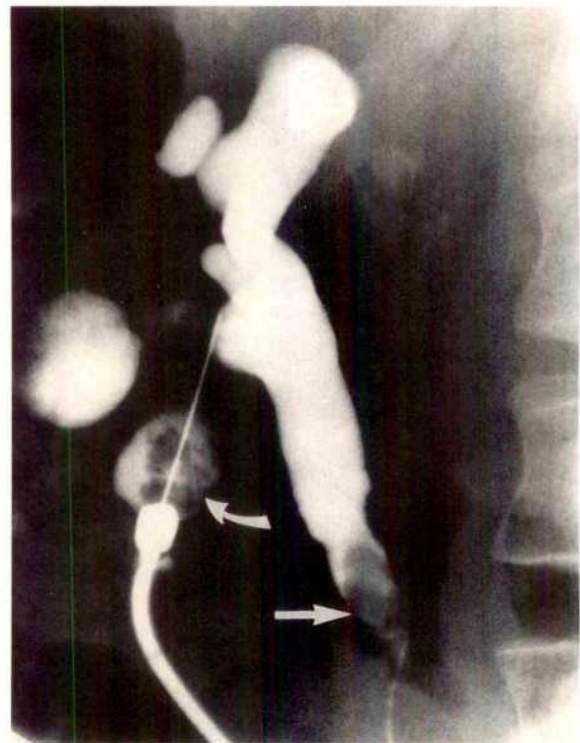


Figure 1. Antegrade pyelogram. A ureteric stone (arrow) is causing obstruction and lower-pole calyceal stones (curved arrow) are shown.



Figure 2. Antegrade pyelogram. The mural-based lesion is a transitional cell carcinoma (arrow).

Haematuria will occur in all patients, rarely requiring transfusion (Ekelund, 1982). Infection is unusual and the incidence is less than that for retrograde pyelography (0.3% versus 6.0%) (Pfister & Newhouse, 1979).

Leaks or obstruction, especially those complicating renal transplants, are particularly important to identify (Figs 4, 5) as both morbidity and mortality are increased (Mundy et al, 1981). The approach to the transplanted kidney should be a lateral one as most are extraperitoneal with the renal pelvis postero-medial. Complications are few, but overdistension of the system causes no pain as the kidney is denervated (Lieberman et al, 1981).

Upper tract urodynamics

The Whitaker test is used to evaluate equivocal obstruction to the upper urinary tract. Dilatation is not

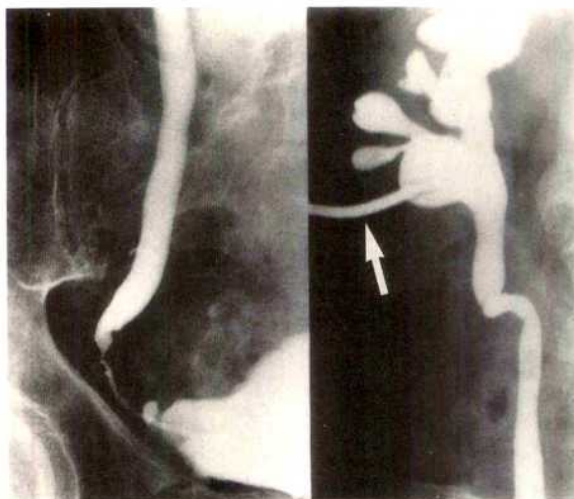


Figure 3. Antegrade pyelogram showing a long and irregular distal ureteric stenosis due to post-radiation fibrosis in a patient treated for pelvic malignancy. Once diagnosed, a percutaneous nephrostomy was inserted (arrow).

synonymous with obstruction and, equally, an undilated system does not exclude obstruction (Maillet et al, 1986). The test involves perfusing the kidney with dilute contrast medium through an antegrade puncture at a known rate whilst simultaneously measuring the pressure within the pelvi-calyceal system and bladder. The test was first described in 1969 (Backlund & Reuterskiöld, 1969), but was popularized in the United Kingdom by Whitaker (1973). Using Whitaker criteria and an infusion rate of 10 ml/min, a pressure of less than 15 cm of water excludes obstruction. A rise in pressure to more than 22 cm of water is diagnostic of obstruction. The test must be done under fluoroscopic control to ensure that there is no extravasation occurring during perfusion. This will erroneously produce lower pressures and invalidates the test.

Percutaneous pyeloscopy

Although a diagnostic procedure, it will be discussed later with tumour ablation and pyelolysis.

Renal biopsy

Renal biopsy must be done under radiological guidance. It is the one organ biopsy that the clinicians have attempted to monopolize. The more enlightened will ask a radiological colleague to identify the lower pole of the kidney with ultrasound after which the biopsy is performed blind.

To put a renal biopsy specimen in formalin renders it almost worthless. To prevent this, liaison with the pathology department is crucial and ideally they should be on hand to receive the specimen.

The indications for biopsy are to establish the cause of renal failure in diffuse disease or to determine the histology of localized renal masses. In the former, the ideal biopsy is of cortical and not medullary tissue. To achieve this, initial assessment of cortical depth is

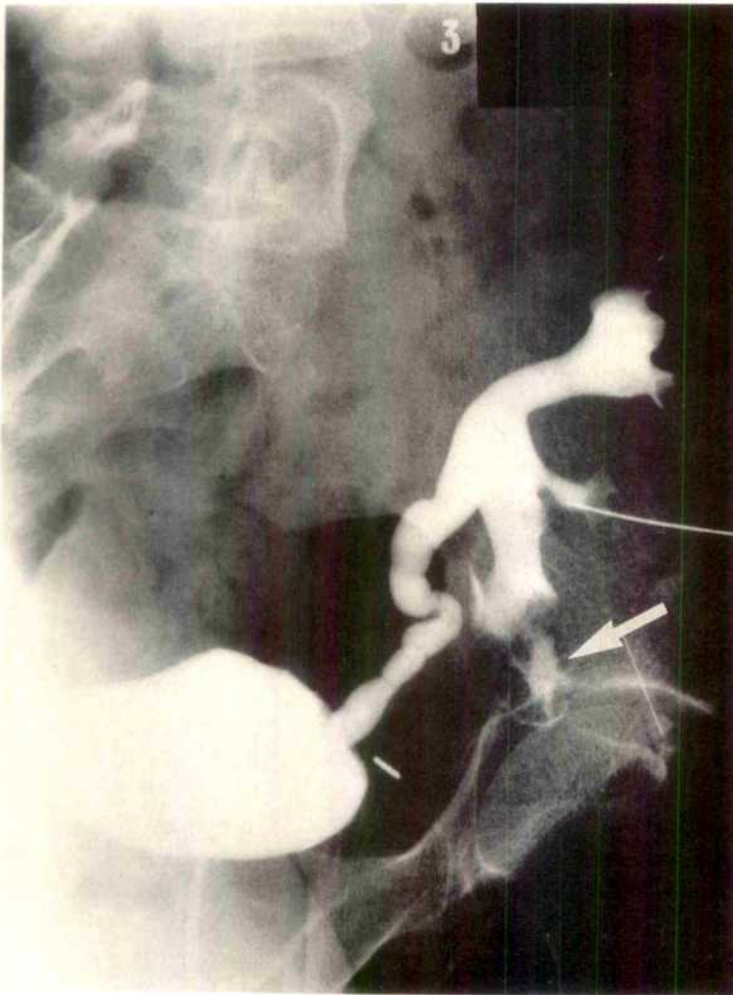


Figure 4

Figure 4. Antegrade pyelogram following renal transplantation in a patient with a persistent leak through a lower-pole calyx (arrow).

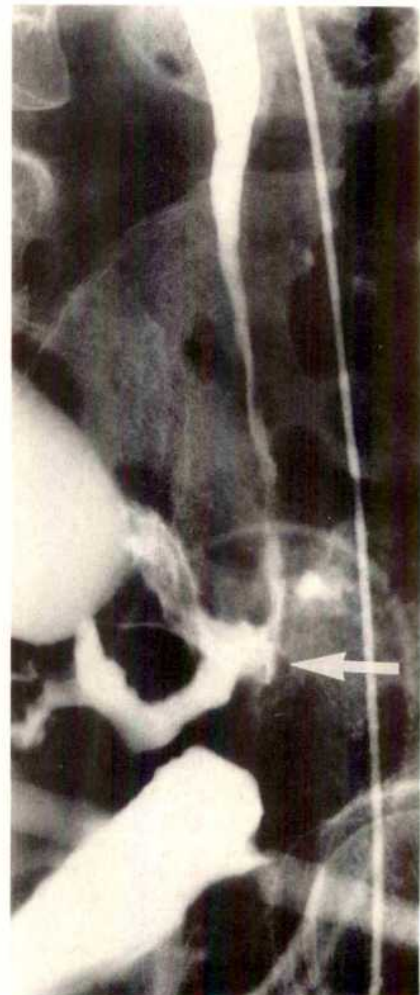


Figure 5

Figure 5. Antegrade pyelogram demonstrating a uretero-colic fistula (arrow).

essential to determine whether a 1 or 2 cm core is appropriate. Under continuous ultrasound guidance, with the patient breathing quietly, the tip of an 18-G biopsy needle (Biopty, Uppsala, Sweden) is positioned over the lower pole in the perinephric fat adjacent to the renal capsule. The biopsy is performed in suspended respiration. This technique is standard irrespective of renal site.

Suspected arterio-venous malformations or aneurysms are absolute contraindications to biopsy. A bleeding diathesis or a single kidney are relative contraindications. Haematuria, flank pain and perirenal haematomas are common, but rarely require specific treatment (Nadel et al, 1986).

Percutaneous nephrostomy

Percutaneous nephrostomy (PCN) was first described in 1955 as an emergency procedure to decompress

obstructed kidneys where retrograde drainage or surgical nephrostomy were either impossible or inappropriate (Goodwin et al, 1955). It is now routine, has specific indications (Table III), has a low morbidity and mortality (Stables et al, 1978) and can be performed on any patient irrespective of their general condition, even at the bedside.

Not all obstructed kidneys require drainage. Most cases of acute obstruction can be managed conservatively, although the presence of an infected system or incipient post-renal failure require immediate

Table III. Indications for percutaneous nephrostomy

1. To relieve obstruction
2. To allow upper tract fistulae and leaks to heal
3. To drain infected kidneys

drainage. Difficulty arises in the patient with obstruction due to irreversible disease, where each case must be individually assessed, specifically in patients with malignant obstruction. Radiologists are often asked to drain the obstructed kidneys of patients with disseminated or localized abdominal and pelvic malignancy. The balance between improving the immediate quality of life, but risking a protracted uraemic death poses a moral dilemma. The ultimate decision rests jointly with the referring clinician and patient (Ortlip & Fraley, 1982).

Leaks and fistulae of the urinary tract are often iatrogenic in origin. Percutaneous nephrostomy may be all that is required to allow them to heal, although additional procedures such as stenting (Lang, 1981) or balloon occlusion of the ureter (Papanicolaou et al, 1985) may be necessary.

Pyonephrosis is usually a complication of obstruction, but can occur without. An increasingly common cause of pyonephrosis follows extracorporeal shock-wave lithotripsy (ESWL). Treatment by PCN is complicated by a collecting system full of infected debris, which impairs visualization. Larger bore drainage tubes are also needed to drain the system adequately.

The various techniques of PCN are well described. Most radiologists feel happy with a modified Seldinger approach using an 18-gauge teflon-sheathed needle for puncture, through which guide wires can be passed and manipulated within the collecting system. The ideal site for puncture is through a lower pole calyx (Fig. 6). This is most easily identified using an antegrade puncture with a 22-gauge spinal needle under ultrasound control and injection of sufficient contrast medium to outline the collecting system. Before a drainage catheter is inserted, a tract needs to be dilated up to at least 2 F larger than the nephrostomy tube, because of the tube redundancy formed when the pigtail end of the tube is straightened. The Seldinger technique ensures that all the catheters' side holes are within the collecting system. This is not easily achieved using a trocar catheter or one-step sheathed needle, which are only suitable for draining markedly dilated collecting systems. In most circumstances, the upper tract can be adequately drained with a 6 F catheter. Should larger tubes be needed, especially after ESWL, 20F is used. There is no point in inserting tubes of intermediate size. Large tubes are usually put in through an Amplatz sheath. Dilating up to 22 F can be done under local anaesthesia and sedation, but general anaesthesia is more appropriate. There is essentially no difference in the technique either in paediatric practice (Irving et al, 1987) or in the transplant patient (Mundy et al, 1981).

Serious complications of PCN are unusual, major vascular injury occurring in 1–2% of cases (Cope & Zeit, 1982). In their review of 300 PCNs, major haemorrhage requiring percutaneous transcatheter embolization occurred in three cases. Septicaemia following PCN for pyonephrosis can be expected in 2% of patients (Cho et al, 1980).

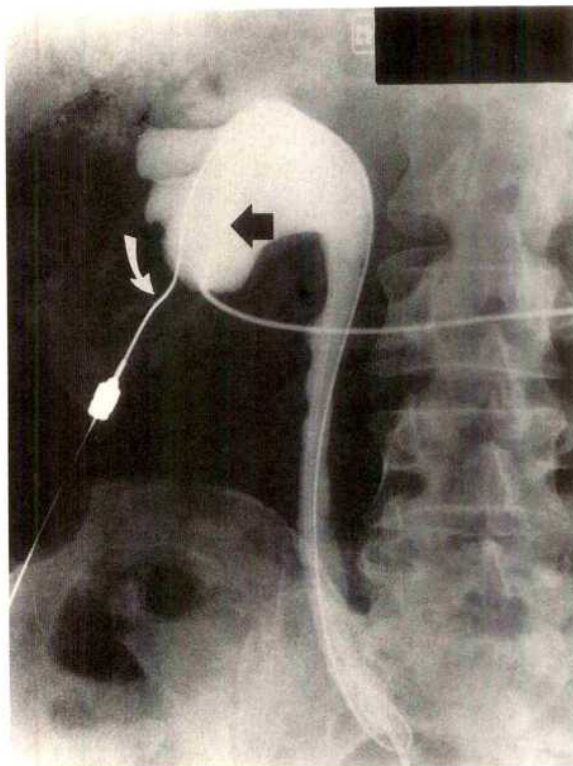


Figure 6. Percutaneous nephrostomy. An antegrade needle has been inserted into the renal pelvis (arrow) and the pelvi-calyceal system is outlined. A lower-pole calyx has been punctured and a guide wire inserted down the ureter (curved arrow). A double 'J' stent is *in situ*.

Percutaneous nephrolithotomy

Non-operative stone removal via a percutaneous approach was first described by Fernstrom and Johansson (1976). The removal of large stones was enhanced by the development of ultrasound and electrohydraulic lithotripsy. This technique has been tested and perfected in the last decade and is of proven value (Wickham et al, 1981; Reddy et al, 1985). Extracorporeal shock-wave lithotripsy now provides strong competition, is non-invasive and does not require general anaesthesia (Brannen, 1986). The availability of ESWL is limited in the UK and not all stones are suitable. Large stones (greater than 2.5 cm in diameter), inability to focus the shock wave on the stone because of body habitus and cystine calculi, which fragment poorly and into large pieces that do not readily pass, are some of the indications for primary percutaneous nephrolithotomy (PCNL). In any event, ESWL cannot be practised in the absence of facilities for PCNL (Leroy et al, 1987). The advantage of PCNL over ESWL is guaranteed complete stone clearance by visual inspection of the pelvi-calyceal system.

The initial steps of PCNL are identical to PCN, but the site of puncture differs depending upon the location

of the stone. For instance, middle-pole calyceal stones cannot be extracted from a lower-pole puncture. Controlled opacification of the upper tract is best achieved by a retrograde catheter placed in the renal pelvis. Dilatation of a tract requires a secure guide-wire position. This may require the use of a pre-shaped catheter, *e.g.* femoro-visceral, to manipulate the wire down the ureter. Serial dilatation up to at least 26 F is necessary to allow instrumentation with a nephroscope. Stones that cannot be extracted piecemeal through a 30 F tract are fragmented with either ultrasound or electrohydraulic lithotripsy. If the procedure is quick and uncomplicated and all stone removed, a nephrostomy tube is not needed. In the case complicated by bleeding or incomplete stone removal, a nephrostomy tube 2 F smaller than the tract is left *in situ* to drain the kidney, tamponade the tract and permit access to the pelvi-calyceal system. The tube is removed once the kidney is stone-free and the upper tract unobstructed on a nephrostogram.

The technique of PCNL is equally applicable to ureteric stones, which can be pushed back into the kidney by retrograde manipulation. Percutaneous nephrolithotomy is always complicated by haematuria, but major complications, specifically bleeding requiring transfusion, can be expected in up to 12% of cases (Lee et al, 1986). Infection, retained stone fragments and pelvi-ureteric junction stricture are also recognized.

Stent insertion and balloon dilatation

The upper tract can be drained internally using double 'J' stents (Finney, 1978) (Fig. 7). This is relevant where long-term drainage is envisaged. The usual indication is obstructive uropathy due to pelvic malignancy or as a consequence of recent post-operative stricture formation. They are also effective in the treatment of acute calculous disease, hydronephrosis in pregnancy and retroperitoneal fibrosis. There are advantages to stenting. The inconvenience of external drainage into a bag is spared and there is less risk of displacement. Disadvantages include migration of the stent and failure to negotiate the obstructing lesion, although an 80% success rate can be expected in malignant obstruction (Evans et al, 1988). Stents should be changed every 3–6 months at cystoscopy (Mitty et al, 1986). Encrustation of the stent is more likely to occur in the stone-former and necessitates changing the stent every 6 weeks (Pocock et al, 1986).

If a retrograde approach at cystoscopy is impossible, an antegrade or combined approach is employed. To facilitate placement of a double 'J' stent antegradely, puncture of a middle-pole calyx decreases the coaxial resistance of the stent over a guide wire. Once the obstructing ureteric lesion has been negotiated and the guide wire placed in the bladder, there is the option of retrograde stenting once the guide wire has been retrieved from the bladder at cystoscopy (Mitty, 1983).

Ureteric strictures can be dilated using balloons (Fig. 8), but this technique is only of proven use in benign strictures (Effersoe & Gammelgaard, 1987).



Figure 7. Bilateral double 'J' stents inserted antegradely to decompress kidneys obstructed by prostate carcinoma. The right stent (arrow) has not been advanced far enough into the bladder. It can be pulled down at flexible cystoscopy, which can be performed under local anaesthetic.

Percutaneous pyeloscopy, tumour ablation and pyelolysis

Pyeloscopy is performed to resolve the question of whether small filling defects seen on excretory urography and unresolved with other imaging techniques are transitional cell tumours. Direct inspection of the urothelium can be done retrogradely with a ureteroscope or antegradely through a PCNL tract.

Percutaneous ablation of upper tract urothelial tumours now has a place. It is performed in patients with impaired renal function where nephro-ureterectomy would be inappropriate. Indications include a single functioning kidney and poor renal reserve in bilateral disease. Patients who refuse conventional surgery or who are poor operative risks might also be considered (Woodhouse et al, 1986). Once the tumours are visualized, they are ablated using diathermy or a neodymium:YAG laser. To avoid dissemination of the disease within the urothelium, pre-operative intracavitary therapy through a nephrostomy

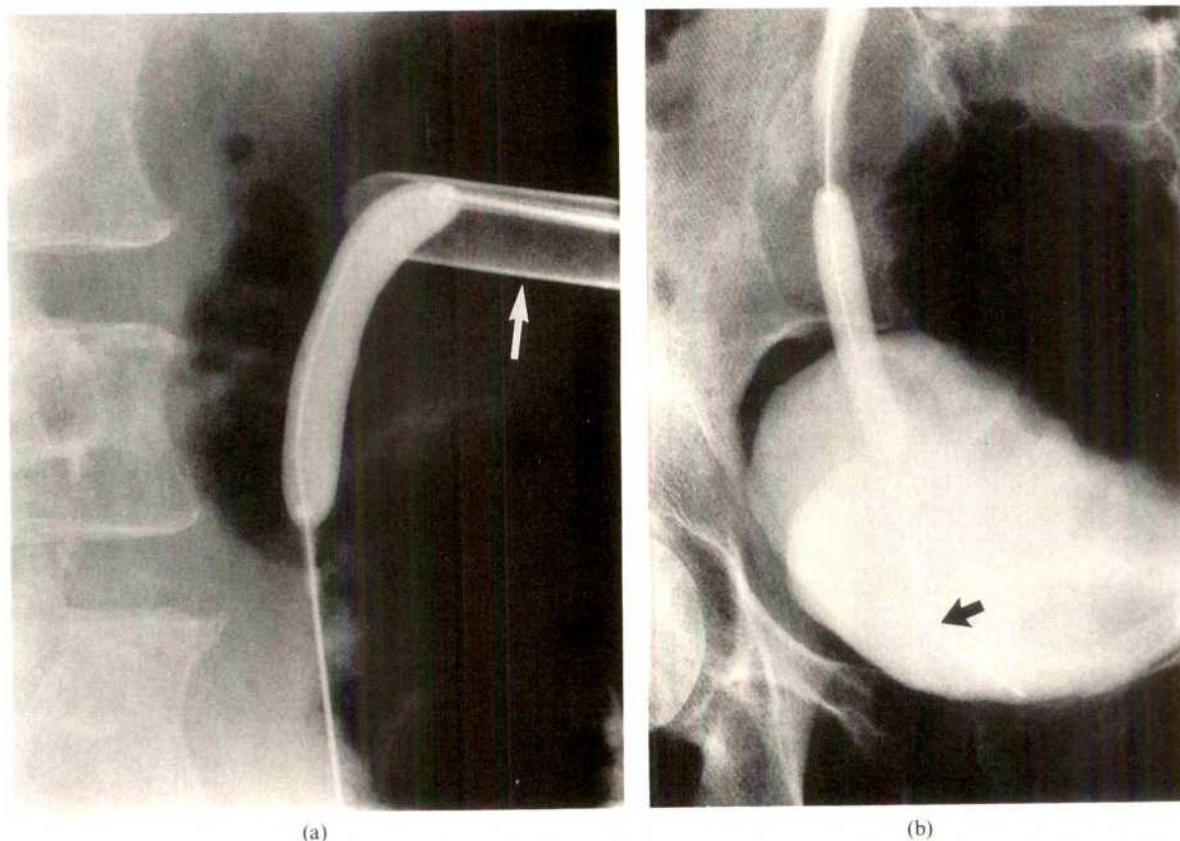


Figure 8. (a) A balloon has been passed through a secondary pelvi-ureteric junction obstruction and inflated. This was done following percutaneous nephrolithotomy for renal stone through a 30 F Amplatz sheath (arrow). (b) A distal ureteric stricture has been traversed by a guide wire (arrow) and balloon dilated.

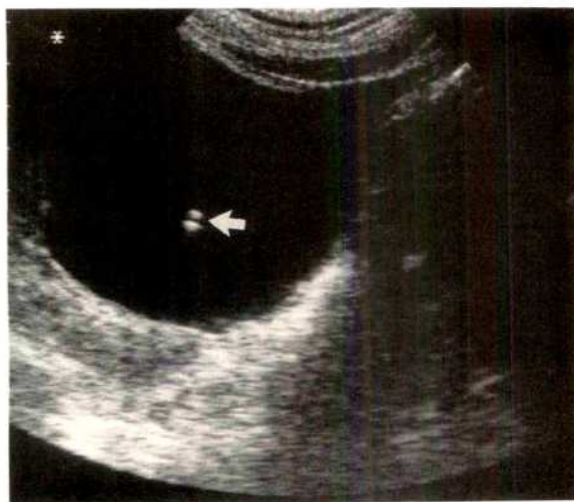


Figure 9. Renal cyst puncture. Under ultrasound control, a needle has been inserted into the middle of the cyst (arrow). The cyst was aspirated because of symptoms resulting from its size.

tube with mitomycin or bacillus Calmette-Guérin (BCG) is performed (Smith et al, 1987).

There are two main complications. First, there is the risk of local tumour spillage and, secondly, of tumour implantation in the nephrostomy tract.

Percutaneous pyelolysis involves incising the pelvi-ureteric junction (PUJ) postero-laterally through a PCNL tract (Ramsay et al, 1984). It is more likely to be of benefit in those with secondary PUJ stenosis rather than primary PUJ obstruction.

Renal cyst puncture

Localized renal cystic lesions are usually benign and of no clinical significance. They have characteristic appearances on ultrasound (Pollack et al, 1982). Complicated cysts, *e.g.* those having irregular outlines, septa, associated with calcification or having internal echoes, warrant further investigation. In the majority, CT will be definitive (McClennan et al, 1979). The diagnostic role of cyst puncture is restricted to those cases that remain equivocal. One indication is the suspected infected cyst that can be difficult to diagnose

with conventional imaging, but can rapidly be resolved with cyst puncture (Bosniak, 1986).

There are two therapeutic indications. By virtue of their size, cysts can be symptomatic; these can be drained completely and sclerosed to prevent recurrence. The asymptomatic cyst in the anxious patient is the only other indication.

The technique for cyst puncture is straightforward using a 15 cm 22-gauge needle and ultrasound control (Fig. 9). Positive bacteriology and/or cytology are conclusive. The appearance of the aspirate and its histochemical analysis is a subject of debate (Lang, 1980; Murphy & Marshall, 1980). It is not our practice to perform double contrast studies of the cyst cavity where both false negative and false positive results have been reported (Jackman & Stevens, 1974). Seeding of the needle tract is very rare (Bush et al, 1977).

The ultimate option is surgery and the willingness of the urologist to accept the imaging evidence provided.

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The radiographic differentiation of pulmonary oedema

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Abstract. A radiographic scoring system has been reported to have a high diagnostic accuracy in the differentiation of pulmonary oedema of renal, cardiac and capillary origin. In the present study, a similar scoring system was used in 51 patients with radiographic appearances of pulmonary oedema due to renal failure ($n=16$), cardiac failure ($n=13$) and to adult respiratory distress syndrome (ARDS) ($n=22$). Evidence of increased pulmonary capillary permeability to transferrin was sought in all patients using a double-isotope method to derive a protein accumulation index (PAI). Using the clinical diagnosis of each type of pulmonary oedema as the "gold standard", sensitivity, specificity and accuracy for the chest radiographic scoring system in pulmonary oedema of cardiac origin were 46, 84 and 75%, respectively. For renal patients these values were 63, 86 and 78% and for ARDS, 89, 33 and 77%. For the PAI in ARDS, sensitivity was 85%, specificity 67% and accuracy 86%. The radiographic scoring system failed to distinguish between pulmonary oedema of renal and cardiac origin and cannot be considered of diagnostic value, but it was more successful in assessment of ARDS. Radiographic appearances suggestive of capillary injury and increased capillary permeability to transferrin occurred in all groups and such findings are not specific to ARDS as currently defined.

The chest radiograph has been used in the assessment of patients with pulmonary oedema since the introduction of radiography, but quantification of radiographic signs of pulmonary oedema is a more recent development. A significant relationship has been demonstrated between extravascular lung water (EVLW) content, measured by indicator-dilution techniques, and specific radiographic appearances in man and animals (Yu, 1971; Milne, 1973; Biddle et al, 1974; Pistolesi & Giuntini, 1978; Snashall et al, 1981). Milne et al (1985) reported differences in appearance between pulmonary oedema of renal, cardiac and capillary origin (adult respiratory distress syndrome (ARDS)) by analysis of scores (graded from 0 to +++) for several radiographic features. A diagnostic accuracy of 91% was achieved in the distinction of pulmonary oedema due to capillary leakage from that due to renal or cardiac failure, with an accuracy of 81% in the distinction between the cardiac and renal patients. These results suggested that more confident radiographic differentiation should be possible between pulmonary oedema developing in association with either increased or normal hydrostatic pressure.

This study aimed to determine the relative sensitivity and specificity of radiographic assessments of pulmonary oedema of renal, cardiac and capillary origin, in a clinical setting, based on chest radiographic scores as reported by Milne et al (1985). In addition, capillary permeability to transferrin was determined in all patients using a double-isotope method (Röcker et

al, 1988). This method has been reported in dogs to have a high specificity for increased pulmonary vascular permeability to plasma proteins following endothelial injury and to differentiate between pulmonary oedema due to increased capillary permeability or to raised hydrostatic pressure (Dauber et al, 1985).

Subjects

Fifty-one patients with clinical and radiographic evidence of pulmonary oedema were studied (Table I); renal failure or fluid overload was present in 16. Patients with fluid overload (three) were included in the renal group, as in the study by Milne et al (1985). Three patients were undergoing regular haemodialysis and three continuous ambulatory peritoneal dialysis. The remaining patients presented with pulmonary oedema in association with acute renal failure. Cardiac failure was present in 13, and was associated with left ventricular failure following acute myocardial infarction (nine), an exacerbation of established left ventricular failure (three) or acute myocarditis (one). Twenty-two patients with a wide range of underlying conditions satisfied criteria for ARDS (Petty & Fowler, 1982). Patient selection was determined by the patient's willingness to undergo a double-isotope study.

Methods

Radiographic scoring

Chest radiographs were taken for routine clinical purposes in an appropriate position. Milne et al (1985) described 10 radiographic features of value in the diagnosis of pulmonary oedema and the frequency of occurrence of each feature. A scoring system was devised for eight of these features (Table II). The subjective assessment of pulmonary blood volume and lung volume were found to be difficult and was

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Table I. Clinical details, summarized as mean (SD), of 51 patients with pulmonary oedema associated with renal failure ($n=16$), cardiac failure ($n=13$) and ARDS ($n=22$)

	Age (years)	Urea (mmol/l)	Creatinine (mol/l)	Alb (g/l)	TProt (g/l)	COP (cm H ₂ O)	PaO ₂ / FiO ₂
Renal group ($n=16$)	46.9 (18.7)	30.4 (13.8)	695 (405)	25.9 (4.7)	59.7 (11.3)	236 (68)	35.0 (13.1)
Cardiac group ($n=13$)	61.9 (9.8)	13.2 (5.1)	148 (23)	28.5 (6.5)	56.3 (9.7)	233 (60)	35.0 (15.4)
ARDS group ($n=22$)	53.9 (18.8)	11.3 (6.8)	167 (169)	23.9 (8.2)	48.9 (7.5)	200 (57)	13.6 (2.9)

Abbreviations: Alb, albumin; TProt, total protein; COP, colloid osmotic pressure; PaO₂/FiO₂, arterial oxygen tension (kPa)/inspired oxygen content (0.21–1.0).

abandoned during preliminary studies. Each radiograph received a cardiac, renal and capillary score. These were derived from scores for features of cardiac, renal and capillary pulmonary oedema weighted for their frequency quoted by Milne et al in 1985 (Table II). For example, a radiograph showing even distribution of pulmonary oedema, inverted pulmonary blood flow,

widened vascular pedicle width, septal lines and effusions would receive a score of 13, 4, 0 for cardiac, renal and capillary features (Table III). The score suggests that the appearances are those of pulmonary oedema of cardiac origin.

With this system, the aim was to satisfy the following requirements.

Table II. The eight radiographic features (from Milne et al, 1985) found to be most useful in classification of pulmonary oedema, the frequency (a) with which each feature occurred in the three types of pulmonary oedema as reported by Milne et al (1985) and (b) the cardiac, renal and capillary scores for each feature that were used in the present study

Radiographic features	Cardiac		Renal/ overhydration		Capillary		Maximum differential score
	(a)	(b)	(a)	(b)	(a)	(b)	
1. Pulmonary oedema							
Homogeneous		1		1		0	
Patchy		0		0		3	3
Central	10%	0	70%	3	20%	1	
Peripheral	0%	-2	0%	-2	45%	3	5
Even	90%	5	30%	1	35%	2	
2. Pulmonary blood flow							
Normal	10%	0	20%	1	40%	2	
Balanced	40%	2	80%	4	50%	3	
Inverted	50%	3	0%	-2	10%	0	5
3. Vascular pedicle width							
< 43 mm	0%	-3	0%	-3	33%	2	5
43–53 mm	40%	2	15%	1	37%	2	
> 53 mm	60%	3	85%	4	30%	2	
4. Septal lines	32%	1	20%	1	0%	-3	4
5. Peribronchial cuffing	80%	3	95%	3	33%	1	2
6. Air bronchogram	20%	1	20%	1	70%	4	3
7. Effusion	38%	1	25%	0	10%	-1	2
8. Heart volume (cardio-thoracic ratio > 50 or < 50%)							
Enlarged	73%	2	85%	3	32%	1	
Not enlarged	27%	2	15%	1	68%	4	3
Maximum potential score		20		20		20	

Table III. Example of scoring for pulmonary oedema features

Feature of pulmonary oedema	Cardiac score	Renal score	Capillary score
Even distribution	5	1	2
Inverted pulmonary blood flow	3	-2	0
Widened vascular pedicle width	3	4	2
Septal lines	1	1	-3
Effusions	1	0	-1
Final score	13	4	0

(1) Consistent scoring of a feature according to the frequency recorded by Milne et al (1985). Inverted pulmonary blood flow and balanced blood flow occurred in 50% of cardiac and capillary pulmonary oedema radiographs, respectively. Hence, in the present study the cardiac score for inverted blood flow and the capillary score for balanced flow were the same (Table II).

(2) To generate the same maximum score for each type of pulmonary oedema if all eight features were present (Table II).

(3) To give an overall weighting based on the three main discriminating features reported by Milne et al (1985). These were variations in distribution of pulmonary oedema, abnormalities of pulmonary blood flow and range of vascular pedicle width, where the maximum differential score was the same (5) and greater than for the other features (Table II). For this purpose, negative scores were used when a specific feature was absent in Milne's study.

A linear scoring system related to frequencies quoted in Milne's study was deliberately avoided as it would introduce inappropriately high scores for some features with limited discriminatory value.

Each radiograph was assessed by two radiologists (A.R.M., D.H.R.), who were unaware of the clinical diagnosis and final scores represented their agreed consensus.

Double-isotope method to determine transferrin accumulation in the lung

A non-invasive double-isotope method was used to determine transferrin accumulation in both lungs (Rocker et al, 1988). *In-vivo*-labelled erythrocytes (technetium 99m, 12 MBq) and circulating transferrin (indium 113m, 20 MBq) were detected externally over the upper anterior zones of each lung and the heart using a single mobile, sodium iodide probe. A protein accumulation index (PAI) for transferrin was derived (Rocker et al, 1988).

Patients were studied as soon as possible after admission and all radionuclide studies were performed within 24 h of the admission chest radiograph.

Colloid osmotic pressure

Colloid osmotic pressure was estimated from serum albumin and globulin concentrations (Keys, 1938).

Data analysis

Because of skewed distribution of the radiographic scores, medians of group data are reported. Kruskal-Wallis analysis of variance was used to assess differences between grouped data. Within-group data were compared using a Friedman two-way analysis of variance. A Spearman rank correlation was used to relate radiographic scores and the PAI. The greater value PAI from a bilateral study is quoted. An analysis of variance was used to assess differences between groups for other clinical variables. Levels of $p < 0.05$ were considered significant.

Results

Radiographic scores

(a) *Renal patients.* The assigned diagnosis, based on the chest radiograph, was correct in 10 out of 16 cases. The median radiographic scores were cardiac 10, renal 14 and capillary 8.5, which favoured a renal cause, but the renal score was not significantly greater than the cardiac or capillary score (Fig. 1). A cardiac cause was suggested for two patients and capillary oedema by three scores. Cardiac and renal scores were identical in one patient.

(b) *Cardiac patients.* The median radiographic scores for the group (cardiac 10, renal 7, capillary 6) indicated a cardiac cause but difference between scores was not significant (Fig. 1). A radiographic score supportive of cardiogenic oedema occurred in only six out of 13 cases. A capillary cause was indicated in three cases, a renal cause in one patient and mixed features in three.

(c) *ARDS (capillary) patients.* The assigned diagnosis by radiographic scoring was correct in 18 out of 22 cases. In four cases the score favoured a renal or cardiogenic cause. Median radiographic scores were cardiac 5, renal 5, capillary 13.5, which was significantly greater than the other two scores ($p < 0.01$, Fig. 1).

Diagnostic sensitivity, specificity and accuracy

Using the clinical diagnosis of each type of pulmonary oedema as the "gold standard", sensitivity, specificity and accuracy for the chest radiograph in pulmonary oedema of cardiac origin were 46, 84 and 75%, respectively. For renal patients these values were 63, 86 and 78% and for ARDS, 89, 33 and 77%.

Protein accumulation index

The PAIs of the renal and cardiac groups were not significantly different ($p > 0.05$, Fig. 2). As reported elsewhere (Rocker et al, 1987), the PAI values for both renal- and cardiac-associated pulmonary oedema were significantly less than for the ARDS group ($p < 0.001$). The proportion of PAIs falling outside the upper 95% confidence limits for healthy volunteers was eight out of 16 for the renal group (six out of 13 for uraemic patients), five out of 13 in the cardiac group and 18 out of 22 in the ARDS group (Fig. 2). For the PAI in ARDS, sensitivity was 85%, specificity 67% and accuracy 86%. There was no significant correlation between the PAI and radiographic scores.

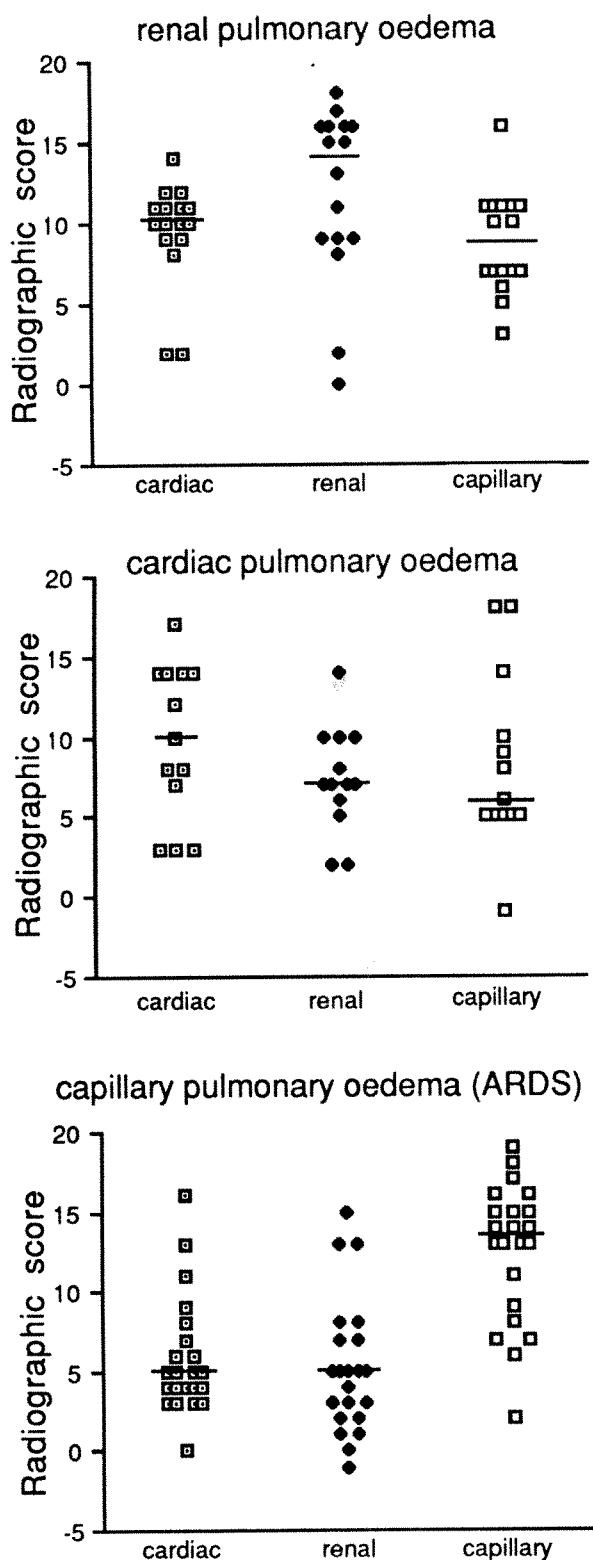


Figure 1. Chest radiographic scores in pulmonary oedema of renal ($n=16$), cardiac ($n=13$) and capillary ($n=22$) origin.

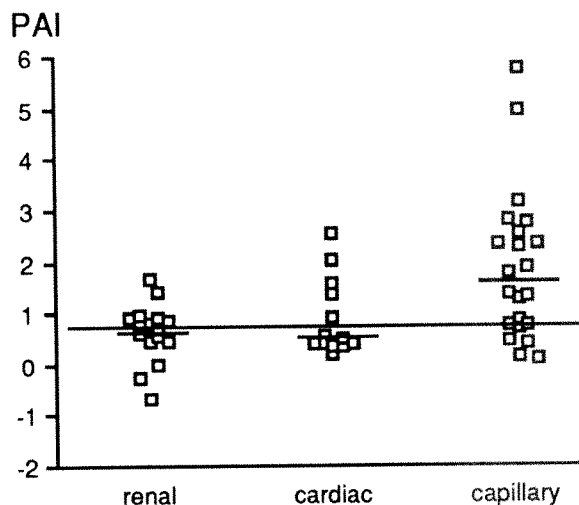


Figure 2. Protein accumulation indices (PAI, $\times 10^{-3}$) in pulmonary oedema of renal ($n=16$), cardiac ($n=13$) and capillary ($n=22$) origin. The group median value and upper 95% confidence limit for healthy volunteers ($n=11$, previously reported in Rocker et al (1987, 1988)) are shown.

Colloid osmotic pressures

The mean albumin concentrations were similar in all groups and not significantly different, although the mean total protein concentration was significantly less ($p<0.01$) in the ARDS than in the renal group. The mean calculated osmotic pressures for the three groups were not significantly different (Table I).

Discussion

The chest radiograph is the simplest non-invasive assessment of pulmonary oedema available to the clinician. Its value in the detection of pulmonary oedema, which may not be apparent on clinical examination, is well established, particularly following myocardial infarction (Logue et al, 1963; Harrison et al, 1971; Chait et al, 1972).

Radiographic scoring, using eight diagnostic radiographic features described by Milne et al (1985), supported the underlying diagnosis for most patients in this study but failed to distinguish between pulmonary oedema of renal and cardiac origin. Scores overlapped and only six out of 13 cardiac patients had appearances characteristic of cardiac origin and four had "capillary-type" pulmonary oedema.

A similar overlap has been demonstrated in physiological studies of pulmonary oedema in man and animals. Alveolar fluid-to-plasma ratios for specific proteins, and of ratios of specific proteins to total protein within the intra- and extravascular space, whilst higher in ARDS, did not give complete separation from patients with cardiogenic pulmonary oedema (Carlson et al, 1979; Sprung et al, 1981). Capillary permeability to proteins of intermediate size (45–72 Å) was similar in cardiogenic and non-cardiogenic pulmonary oedema (ARDS) but, in patients with ARDS, capillary

permeability had increased sufficiently to allow larger proteins (>72 Å) to leave the intravascular space (Sprung et al, 1987). Histopathological studies also suggest that there is considerable disruption of the alveolar capillary barrier in patients dying with cardiogenic pulmonary oedema (Katelnitskaya et al, 1983), which is not always associated with a raised left atrial pressure (Biddle et al, 1974; Timmis et al, 1981).

In this study, pulmonary accumulation of transferrin was lower in pulmonary oedema of renal or cardiac failure than in ARDS, despite similar intravascular albumin concentrations and colloid osmotic pressures in the three groups. However, there was overlap of the protein accumulation index between groups and between patients with pulmonary oedema and a normal control group. This confirms other findings with this method (Braude et al, 1986; Rocker et al, 1987). The insignificant correlation between the PAI and capillary score was not unexpected. Radiographic features of a capillary oedema resolve slowly but episodes of increased capillary permeability to macromolecules may be only transient (Braude et al, 1986). In addition, capillary appearances might be similar, however severe the protein leakage from capillaries.

Radiological scoring and the PAI did not separate renal- and cardiac-failure-associated pulmonary oedema. The twofold greater scores and PAI in ARDS suggest that pulmonary oedema due to microvascular injury can be distinguished radiographically, and by increased permeability to transferrin, from pulmonary oedema due mainly to increased extravascular sodium and water. However, it appears that radiographic appearance and increased capillary permeability to transferrin are not specific to ARDS as currently defined.

This study demonstrated that specific features present on a chest radiograph could not be used to distinguish between pulmonary oedema due to renal or cardiac failure. In practice, there should be additional clinical information to allow this separation. Adult respiratory distress syndrome may be identified with more confidence but "capillary-type" appearances and increased capillary permeability to transferrin were not specific to established ARDS.

Acknowledgment

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X-ray dual-photon absorptiometry: a new method for the measurement of bone density

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Abstract. A recently introduced method (dual-photon X-ray absorptiometry, DEXA) capable of measuring skeletal density in man (at present in the spine and hips, but ultimately for the whole body) has been evaluated in terms of its ability to perform long-term assessment of bone density changes. The method, which uses X rays rather than γ rays as its photon source, represents a significant improvement over present systems both in image quality and precision (reproducibility) of results, which is better than 1% *in vivo*. Scanning time is approximately halved compared with present techniques and the radiation dose is reduced by 25%. First data on long-term drift of results and effects of changes in patient composition (*i.e.* thickness and fat content) are given and show the new method to be superior to present radionuclide systems. It is likely that this new method will become the standard for bone density measurements.

Osteoporosis has been described as the commonest of all diseases (Jackson, 1955). In this condition, bone mass decreases and the skeleton becomes more prone to fracture. It is now well known that post-menopausal or oestrogen-deficient women are at particular risk (Lindsay et al, 1976). There is a 20-fold increase in expected mortality for women over the age of 40 years sustaining a fracture of the neck of femur (Lewis, 1981; Fogelman, 1985).

Many methods have been used to assess bone density, the most widespread being based on the attenuation of either single (SPA)- or dual (DPA)-energy γ rays. The attenuation is related to the amount of material through which the rays pass and its density. *In vivo* it is assumed that the body consists only of soft tissue and bone, and the amount of bone is calculated. If the thickness of soft tissue is constant throughout the scanned region, then a single γ -ray energy is sufficient for the calculation; in the case of SPA of the forearm this situation is achieved by placing the arm in a water bath. For regions where the soft tissue is of variable thickness, two γ rays of different energy are required and their relative attenuation is used to calculate the amount of bone present and eliminate the effect of soft tissue. This is the method currently used to measure the density of the lumbar spine and femur, the two γ rays normally being produced by a source of gadolinium 153. Typical scanning time for four lumbar vertebrae using a gadolinium-based machine is 20 min. Problems arise because of drifting of results as the source decays; the cost of source replacement depends on the activity required but is approximately £4000 and is typically carried out every 2 years. Further details of these two methods can be found in review articles (Wahner et al, 1984a,b).

This paper reports an entirely new method to detect and measure bone loss, which is likely to replace dual-photon absorptiometry as the reference method for the detection of osteoporosis. The method is based on the measurement of the relative absorption of two, different energy, X-ray beams that pass through the patient. The rays are produced by a low-current X-ray tube, which switches accelerating voltage synchronously with the mains frequency. The use of an X-ray tube rather than the traditional radionuclide source allows a much higher photon flux to be generated and hence much finer collimation to be employed. This results in high-resolution images (Fig. 1) with a concomitant improvement in accuracy of the detection of bone edges.

Bone mineral measurements fall into two broad categories:

1. Absolute measurements against a normal range for diagnosis of disease and assessment of the likelihood of fracture.
2. Longitudinal, relative measurements to assess progression or response to treatment.

Most studies concentrate on the second type of assessment and we have investigated the ability of this method to perform these measurements.

Materials and methods

This new instrument (Hologic QDR1000) (Sartoris et al, 1988) differs from conventional dual-photon bone densitometers in two main ways. First, the photons are produced by a switching X-ray tube synchronized to the mains frequency, such that during each cycle the X-ray tube is supplied alternately with accelerating voltages of 70 and 140 kV. The photon beam passes through a collimator (1 mm diameter) followed by a filter wheel consisting of three portions (air and two sections of epoxy-resin-based materials representing bone and soft

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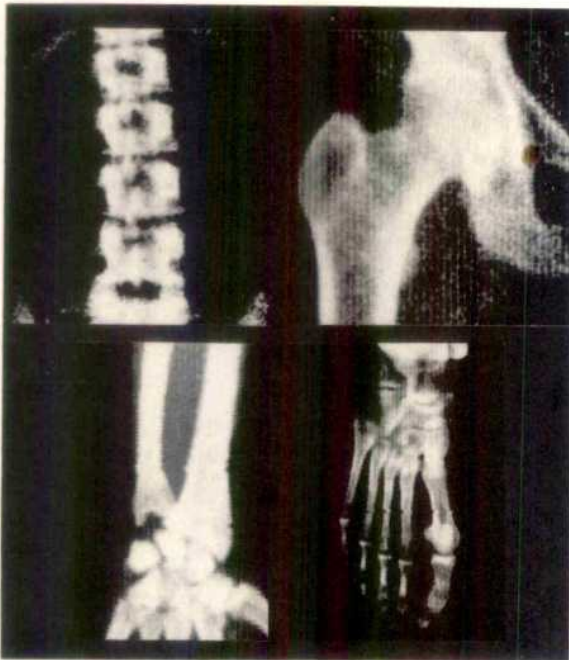


Figure 1. Bone mineral images from the QDR1000.

tissue) and spinning synchronously with the mains frequency and hence the tube's accelerating voltage. This filter wheel allows continuous on-line calibration of the system. Secondly, energy discrimination is not used in the detector because only one energy source is present at a time. The detector simply integrates all the energy

received, yielding a signal proportional to count rate. A schematic diagram of the system is shown in Fig. 2.

The object is scanned by the source and detector moving together in a raster pattern across a stationary bed in a manner similar to conventional densitometers, but as data acquisition rate is tied to the mains frequency only one scanning speed is used, producing measurement of, for instance, four lumbar vertebrae in approximately 10 min.

After a scan is completed, areas of bone and soft tissue are identified automatically by the machine based on the density of each pixel; these areas may be modified by the operator if required. From the areas of bone, the operator can mark the regions of interest (ROIs) required, and in the case of the spine we use the lumbar vertebrae 1-4. Calculations of total bone mineral content (BMC, g) and bone mineral per unit area scanned (BMD, g cm^{-2}) are then made for each ROI.

Although the instrument is able to measure both the lumbar spine and hips (and will be upgraded to allow whole body imaging), this first study was limited to evaluating its ability to perform longitudinal studies on lumbar spine density. The parameters investigated were:

1. Reproducibility (precision) of results.
2. Long-term drift of results.
3. The effect of changes of patient thickness and position.
4. The effect of changes of patient fat content.

Results from measurements obtained using a radionuclide-based system (Novo BMC23) are quoted for comparison with those from the QDR1000.

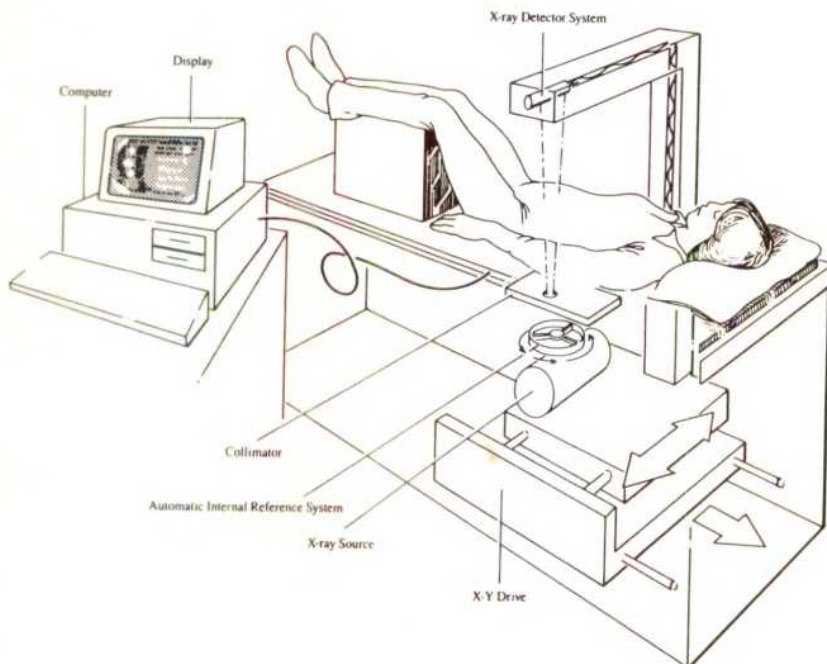


Figure 2. Schematic diagram of the QDR1000.

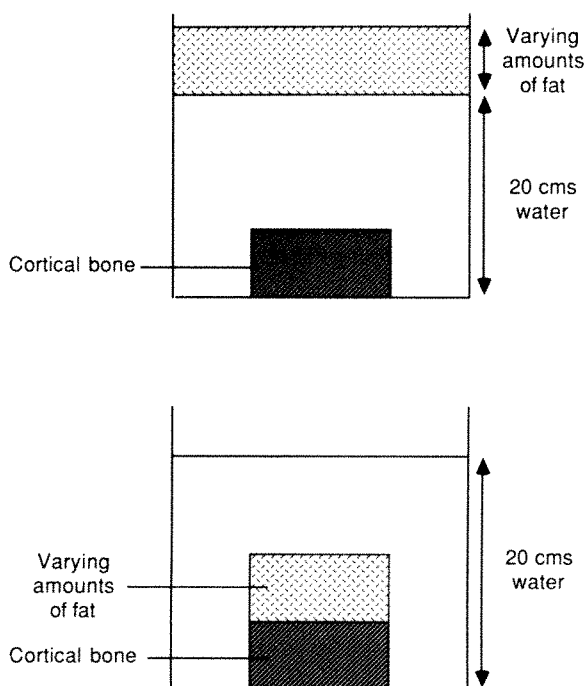


Figure 3. Experimental set-up for measurement of the effect of fat.

Precision

The precision achievable is dependent both on the machine and the object being measured, and is limited by statistical error of the signal, the accuracy of the detection of the bone edge and the reproducibility of object positioning.

The best precision is expected on a regular test object (where the edge detection is simple and repositioning errors negligible) and represents purely statistical variations. This was tested by performing 10 repeat scans on a series of rectangular slabs of different density bone-equivalent material placed in a 15 cm deep water bath. The experiment was repeated for one bone density and various depths of water to investigate the effect of patient thickness on precision.

To include the effect of variability in the detection of the edge of a complex shape, the measurement was repeated with an anthropomorphic spine phantom of realistic bone density and soft-tissue thickness.

Finally, *in vivo* precision, which includes the further effect of patient repositioning, was measured by studying a series of normal volunteers 10 times over a period of 4–6 weeks.

Long-term drift

Longitudinal studies may be continued over a period of several years and so there should ideally be no drift in the results from the machine over long periods of time. A less satisfactory method of dealing with this problem is to monitor the drift and correct results for it. The

Table I. Coefficient of variation for different bone densities

Measured bone density (g cm^{-2})	Coefficient of variation (%)
0.179	1.74
0.356	0.52
0.518	0.48
0.717	0.29
1.073	0.27
1.458	0.17
1.806	0.22

spine phantom has been measured daily throughout a period of 6 months to assess drift.

Patient thickness and position

As well as having a possible effect on the precision of measurement, variations with time in a patient's antero-posterior (AP) thickness may also affect the absolute value of the result. This was investigated by measuring a slab of bone-equivalent material of realistic bone density immersed in different depths of water (simulating different patient thicknesses). Measurements were also made with the slab at different vertical heights from the couch to monitor the sensitivity of the results to patient position.

Fat content

With time, a patient's fat content can alter either uniformly across the whole body or irregularly (*i.e.* fat replacing bone marrow). The effect of these two types of variation was measured using a block of bone-equivalent material placed in 20 cm of water. The former situation was simulated by adding increasing amounts of animal fat to the top of the water bath, whilst investigation of the latter effect utilized slabs of fat-equivalent material placed only over the bone slab. The experimental set-up is shown in Fig. 3.

Results

The precision is quoted as the standard deviation of the repeated measurements expressed as a percentage of their mean (coefficient of variation, CV). Values found for the blocks of differing bone density in 20 cm of water are listed in Table I and show increasing precision with increasing density. The measurement precision is better than 0.5% throughout the clinically expected range ($0.4\text{--}1.4 \text{ g cm}^{-2}$). As shown in Table II, the precision

Table II. Coefficient of variation for different depths of water at a bone density of 1.2 g cm^{-2}

Depth (cm)	Coefficient of variation (%)
2.0	0.14
15.0	0.32
20.0	0.71
25.0	1.43
30.0	3.19

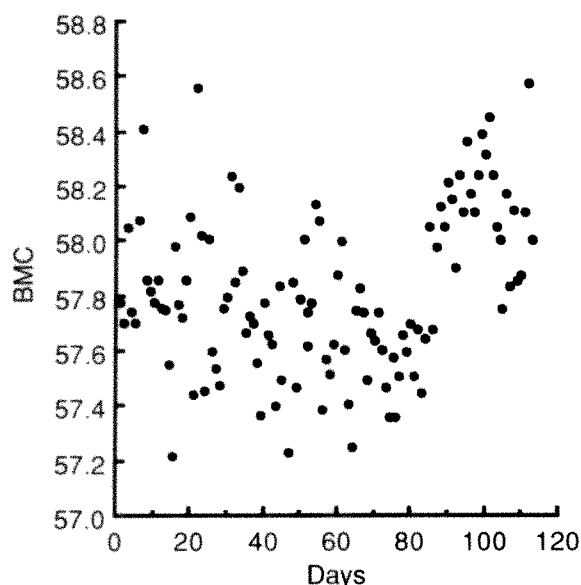
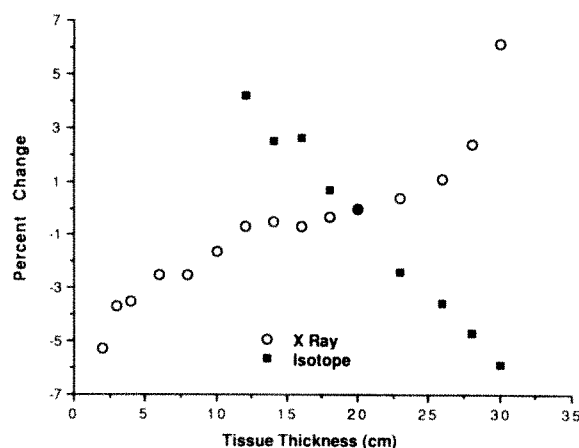
Table III. Coefficient of variation for *in vivo* precision

Bone mineral density (g cm^{-2})	Coefficient of variation (%)
0.841	0.98
0.908	1.70
0.948	0.84
0.983	0.83
1.018	0.97
1.028	0.96
1.060	0.74
1.159	0.53
1.326	0.65

off quite quickly with increasing soft-tissue thickness, reaching over 3% for 30 cm of water compared with a value of 0.7% at 20 cm, a "normal" adult thickness. The inclusion of a non-uniform edge, produced by the anthropomorphic spine phantom, caused a slight increase in measurement CV to a value of 0.45% for a 15 cm thick object. The increase over the value for the bone slab represents the variability of the edge detection algorithm. The bone density and measurement CV for the normals are listed in Table III, all but one volunteer showing a CV below 1%. The increased CV over that measured with the spine phantom is presumably caused by variations in patients positioning from measurement to measurement.

The long-term drift of the machine has been assessed by daily measurement of the BMC for the spine phantom, and the results are shown in Fig. 4 for the 6 months that the machine has been in use.

The effect of varying soft-tissue thickness is shown in Fig. 5, where the results are expressed as percentage

**Figure 4.** Long-term measurements of the spine phantom.**Figure 5.** Effect of soft-tissue thickness.

changes compared with the value obtained in an average (20 cm thick) patient. The bone-density measurement obtained from the QDR1000 are independent of patient thickness except for the very thin (below 10 cm) or the very fat (above 28 cm) subject.

Figure 6 shows the QDR1000 system to give results that are independent of the vertical position of the source. Figures 5 and 6 also include results obtained from equivalent measurements made on a Novo BMC23 gadolinium-based system.

The effect of uniform deposition of adipose tissue over a 20 cm soft-tissue thickness is shown in Table IV and indicates that there is no change in measured bone density except at probably unrealistic depths (above 4 cm of fat). However, the results for non-uniform fat deposition, which are expressed in Fig. 7 as percentage changes from the value obtained with no fat present, indicate a significant effect, an apparent 1% change of bone density being produced by replacing 3 mm of soft tissue with fat.

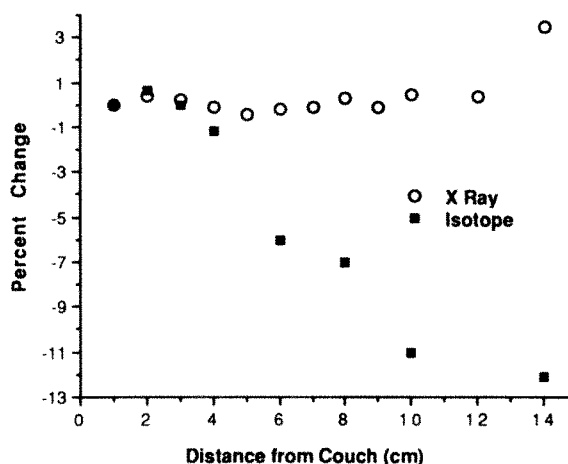
**Figure 6.** Effect of source position.

Table IV. Effect of uniform fat deposition

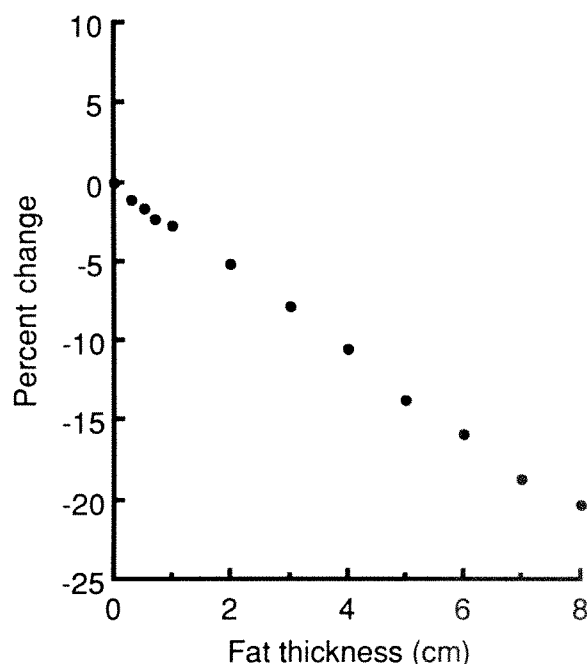
Depth of fat (cm)	Bone mineral density (g cm ⁻²)
1	1.239
2	1.231
3	1.229
4	1.260
5	1.316
6	1.421
7	1.537

Discussion

Many methods have been proposed to assess bone density and longitudinal changes in it. These range from very simple methods able to measure at only one site (single-photon absorptiometry) to quantitative transmission computed tomography offering a three-dimensional representation of density anywhere in the body. Between these extremes lies dual-photon absorptiometry which, while not offering a three-dimensional representation, is applicable to any site and has become the "standard" measurement technique.

Most clinical protocols involving the measurement of bone density require longitudinal evaluations, and hence reproducibility (precision) of measurement is important, especially as changes as small as 2% or 3% per year are significant. Long-term precision can be affected both by variations in the machine and the patient, and a satisfactory technique must be versatile enough to deal with both of these. Short-term precision is affected only by the machine and patient repositioning.

The measurements described in this paper show the new method to represent a significant improvement over previous techniques and are in broad agreement with those made by other groups (Wahner et al, 1988). Compared with radionuclide DPA, the system is less susceptible to variations in patient parameters (thickness and position, Figs 5 and 6) and shows better short-term *in vivo* precision. The single most important performance parameter is the *in vivo* precision, and only changes between scans of two or three times this value can be classed as significant in longitudinal studies. For radionuclide DPA systems, precision is between 2% and 3%, whilst the QDR1000 system has shown better than 1% precision in all but one of the volunteers measured (the data from this volunteer are being further investigated to find the reason for the large variations). These improvements in *in vivo* precision are probably mainly due to better resolution allowing more accurate repositioning of ROIs, while changes in patient parameters have less effect because of the much lower content of scattered radiation in the measured signal. The balance between obtaining sufficient photons for good statistical accuracy and limiting the beam size for good resolution is dependent on the amount of material through which the beam must travel. Hence, at larger tissue thicknesses the statistical error will increase

**Figure 7.** Effect of non-uniform fat deposition.

(Table II). However, the choice of collimator size seems to have been well made for normal patient thicknesses; any reduction in beam size would almost certainly significantly degrade the results because of statistical effects.

Conclusion

The results from the QDR1000 system show that bone mineral density (BMD) can be measured with a precision of better than 1% *in vivo*; however, it must be stressed that these measurements were made on normal volunteers, none of whom had a low density where poorer precision may be expected. Drift (at least over the 6-month period of use) is not significant. Changes in patient AP thickness over a wide range will not affect longitudinal studies and are irrelevant, except possibly in the case of children (under 10 cm, although extra soft-tissue-equivalent material can be added) or very obese patients (over 28 cm). However, thicker patients are measured with less precision. The measurement precision seems to be affected approximately equally by statistical fluctuations in the measurements and patient repositioning errors.

Uniform deposition, or reduction, of adipose tissue will not affect the results except at probably unrealistic thicknesses (above 4 cm), but non-uniform deposition such as is caused by bone marrow being replaced by fat may cause significant changes in the measurement, a 1% change being caused by a replacement of 3 mm of soft tissue with fat.

Therefore, we conclude that with this new technique a

significant advance over the conventional dual-photon radionuclide densitometers has been made. The QDR1000 system is capable of reliable long-term bone density measurement of the lumbar spine within a precision of 1%. Scanning times are reduced to 10 min for the measurement of four lumbar vertebrae and radiation exposure to the patient is slightly lower than with radionuclide systems. The increased image resolution allows better detection of the vertebral edges, intervertebral spaces, fracture lines and compression fractures and hence more reproducible location of regions of interest. These advantages are very important in day-to-day practice. Conventional radionuclide-based systems may now become obsolete.

Before being able to diagnose osteoporosis (as opposed to assessing longitudinal changes within a patient), it will be necessary to produce a range of normal values. However, the calibration procedure applied to densitometers may allow normal ranges derived from radionuclide-based DPA systems to be used, but if not, the large number of QDR systems now in clinical use (in excess of 100) should allow a database to be produced rapidly.

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Total or partial percutaneous renal ablation in the treatment of renovascular hypertension: radiological and clinical aspects

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Abstract. In 15 patients with renovascular hypertension, considered unsuitable for angioplasty or surgery, percutaneous renal ablation was performed by injection of ethanol into the renal vasculature. Partial or complete renal ablation was confirmed by follow-up intravenous pyelography or arteriography. Patients were followed-up for a mean of 24.8 months after therapy and blood pressure was improved in all patients with five being cured. This study shows that percutaneous renal ablation is a useful and successful method of therapy for renal hypertension, and that it should be considered in patients unsuitable for surgery or angioplasty.

Percutaneous renal ablation has been performed in patients with renal carcinoma (Bergreen et al, 1977; Singass et al, 1979; Wallace et al, 1981; Rabe et al, 1982), in transplanted or haemodialysed patients with severe renovascular hypertension (McCarron et al, 1976; Nanni et al, 1983; Fletcher et al, 1984), and in uraemic patients with heavy proteinuria (Henrich et al, 1976; May et al, 1981).

We have previously shown the efficacy of percutaneous renal embolization in patients with renal hypertension (Dal Canton et al, 1984; Russo et al, 1988). In this study, we report a larger series of cases with a longer follow-up period, emphasizing the radiological aspects of the procedure.

Materials and methods

Fifteen patients were included in the study. The clinical and radiological data are reported in Tables I and II. In all patients, clinical assessment included rapid sequence intravenous pyelography and aortography in addition to routine investigations. Where it was possible to discontinue antihypertensive therapy, peripheral plasma renin activity (PRA) and renal vein renin were measured.

Patients were selected for percutaneous renal ablation when percutaneous transluminal angioplasty was technically impossible to perform because of the nature and/or location of the obstructive lesions and when there was an indication for a total nephrectomy but the patient was regarded as being at high risk. Informed consent was obtained from all patients or parents, after discussion of the possible risks and benefits of the procedure.

Percutaneous renal ablation was performed following a selective renal arteriogram. A solution of absolute ethanol (99%) and sodium iohalamate (Angio-Conray 80%; Bracco) was injected into the cannulated vessel under fluoroscopic control. The solution was injected through the main artery of patients with arterial stenosis, while in patients with renal artery occlusion the solution was injected through collateral vessels (provided there was no evidence on a sub-selective arteriogram that they supplied the spinal cord) or, if they were not suitable, through the main renal artery following percutaneous recanalization using a 5 F catheter (Fig. 1). Finally, in patients with intraparenchymal dysplasia, the embolizing solution was injected through the segmental branches.

Bupivacaine (1 ml Marcaine 0.5%) was injected prior to ablation to reduce the pain due to renal infarction. Care was taken during the procedure to avoid reflux of the embolizing solution. This was achieved by adding 1-2 ml of sodium iohalamate (ratio 1:8) to ethanol. It was therefore possible to visualize all phases of the procedure under fluoroscopic control and detect any reflux into the aorta caused by a decrease in arterial blood flow. The injection of sclerosant was given manually, so that the injection rate could be changed during the procedure. In patients with high arterial blood flow, reflux was avoided by using an occlusive balloon catheter. Finally, in patients with severe stenosis of the renal artery, with stenosis located in segmental branches, or when an arterial recanalization was performed before the embolization, the solution was injected through a percutaneous catheter held in wedge position.

After injection, aortography was repeated and, if a residual arterial flow was observed, an additional dose of ethanol was injected. Without further arterial puncture, aortography was performed again 1 h after the embolization to verify the success of the necrotizing procedure. This was demonstrated either by the absence

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Table I. Clinical data of 15 patients treated by percutaneous renal ablation

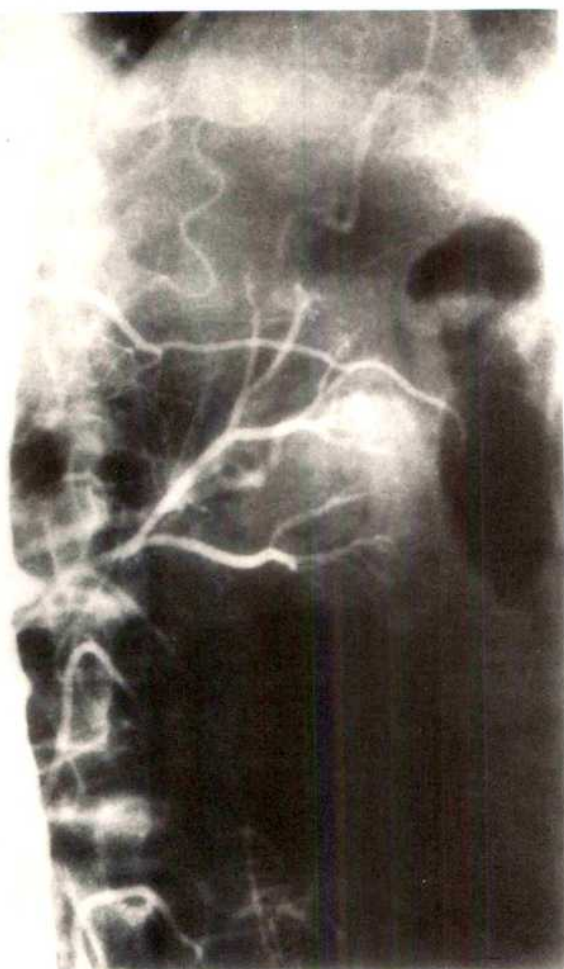
Case	Sex/Age	Duration of hypertension (years)	Percutaneous renal ablation supine/standing (ng ml ⁻¹ h ⁻¹)	Renal vein renin ratio	Target organs lesion ^a
1	F 24	8	0.7/3.7	>1.5	LVH, Grade III fundi
2	M 44	6	0.7/0.8	>1.5	LVH, Grade III fundi, CAD, CVA
3	M 54	6	26/27	—	LVH, Grade III fundi, CAD, CVA
4	M 58	11	13.3/16.5	—	LVH, Grade III fundi, CAD
5	M 64	6	19.3/32.0	—	LVH, Grade III fundi, CAD, CVA, PVD
6	F 50	25	7.0/10	>1.5	LVH, Grade III fundi, CAD
7	M 7	1	4.0/4.0	>1.5	LVH, Grade III fundi
8	F 13	2	2.0/7.0	>1.5	LVH, Grade III fundi
9	F 29	5	8.4/24.5	>1.5	LVH, Grade III fundi
10	M 53	1	—	—	LVH, Grade III fundi, CAD, PVD
11	M 44	1	1.4/3.3	—	LVH, Grade III fundi, CAD
12	M 75	5	5.7/9.6	—	LVH, Grade III fundi, CAD
13	M 68	8	—	—	LVH, Grade III fundi, CAD, PVD
14	M 61	1	—	—	LVH, Grade III fundi, CAD, PVD
15	M 60	2	—	—	LVH, Grade III fundi, PVD

^aLVH, left ventricular hypertrophy; CAD, coronary artery disease (ECG, chest radiograph); CVA, cerebrovascular accident; PVD, peripheral vascular disease.

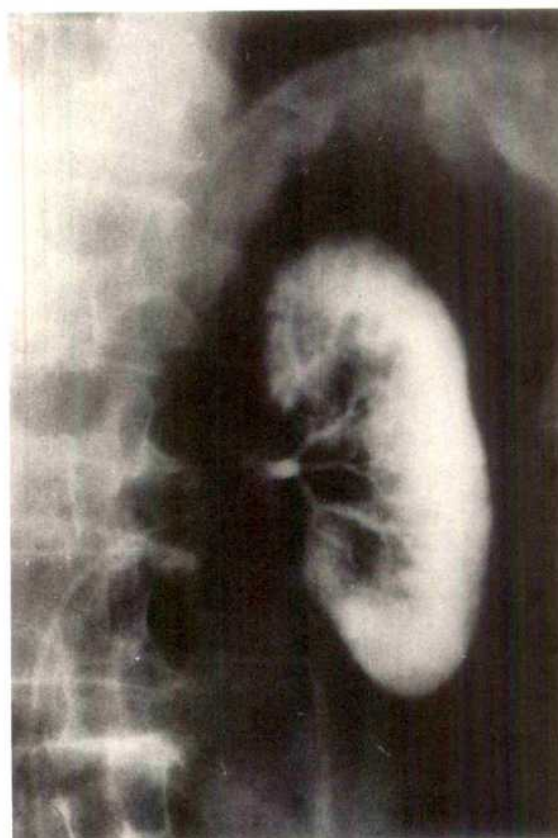
Table II. Radiological features and type of treatment

Case	Length difference between the two kidneys (cm)	Arteriographic features	Embolization material	Treatment
1	11	Right renal hypoplasia	Ethanol, sodium iothalamate	Main renal artery
2	6	Stenosis (90%) right renal artery (A)	Ethanol, sodium iothalamate	Main renal artery
3	5	Thrombosis left renal artery	Ethanol, sodium iothalamate	Collateral vessels
4	7	Thrombosis left renal artery	Ethanol, sodium iothalamate	Collateral vessels, polar renal artery
5	5.5	Thrombosis left renal artery, stenosis right artery (A)	Ethanol, sodium iothalamate	Recanalization of left renal artery, percutaneous transluminal angioplasty of right renal artery
6	3.5	Thrombosis right renal artery, stenosis left renal artery (A)	Ethanol, sodium iothalamate	Main right renal artery, percutaneous transluminal angioplasty of left renal artery
7	—	Stenosis intralobular branches (F)	Ethanol, sodium iothalamate	Partial embolization of lower pole
8	—	Stenosis intralobular branches (F)	Ethanol, sodium iothalamate	Partial embolization of upper pole
9	3	Stenosis right renal artery (F)	Ethanol, sodium iothalamate	Main renal artery
10	5	Stenosis right renal artery (A)	Ethanol, sodium iothalamate	Main renal artery
11	5	Thrombosis right renal artery	Sodium iothalamate	Recanalization main right renal artery
12	2	Thrombosis left renal artery, stenosis right renal artery (A)	Ethanol, sodium iothalamate	Collateral vessels, percutaneous transluminal angioplasty
13	5	Stenosis right renal artery (A)	Ethanol, sodium iothalamate	Main renal artery
14	5	Stenosis (90%) right renal artery (A), stenosis (60%) left renal artery (A)	Ethanol, sodium iothalamate	Main renal artery, percutaneous transluminal angioplasty of the left renal artery
15	5	Stenosis left artery (A)	Ethanol, sodium iothalamate	Main renal artery

A, atheromatous; F, fibrodysplastic stenosis.



(a)



(b)

Figure 1. (a) Abdominal aortography (Case 5) showing the left renal artery is occluded at its origin. (b) Control 1 h after left renal ablation, performed after recanalization of the artery.

of arterial flow to the embolized renal area, or by a long-lasting opacity on the plain standard radiograph. After embolization, patients were closely monitored until discharge, the duration of the stay being between 7 and 14 days. They were then followed-up as outpatients with regular blood pressure measurement, physical examination and routine analysis. Permanent renal ablation was confirmed by intravenous pyelography or digital venous subtraction arteriography 4 months after the procedure.

The patients were regarded as "cured" when their blood pressure was normalized ($\leq 150/90$ mmHg) without antihypertensive therapy and as "improved" when blood pressure was $\leq 150/90$ mmHg with the same or reduced antihypertensive therapy.

Plasma renin activity was measured in blood samples drawn after 8 h in the recumbent position and after the patient had been standing and mobile for 2 h. Normal values for our laboratory are: $0.5\text{--}1.5$ ng ml⁻¹h⁻¹ in supine and $1.5\text{--}3.0$ ng ml⁻¹h⁻¹ in standing positions, respectively. The renal vein renin ratio was calculated by

dividing the plasma renin activity in the renal vein of stenotic or thrombosed by that in the unaffected kidney.

Results

The effects of renal embolization on blood pressure are reported in Table III. At the time of discharge after percutaneous renal ablation, mean systolic blood pressure fell significantly from 190 ± 26.2 (SD) to 134 ± 11.1 mmHg, and mean diastolic blood pressure fell from 118.7 ± 11.0 to 77.8 ± 11.2 mmHg; four patients were "cured" and 11 "improved". At the last control (24.8 months after embolization), mean systolic and diastolic pressure were 134 ± 14.5 and 81.3 ± 8.3 mmHg, respectively; five patients were "cured" and 10 "improved".

A permanent renal ablation was confirmed in 14 patients during follow-up; in one patient with stenosis of an intralobular branch (Case 7), the embolization was repeated 5 months later, intravenous pyelography having shown a normal nephrogram.

Table III. Effects of renal embolization on blood pressure

Case	Before embolization		At discharge after embolization			Follow-up after embolization		
	Blood pressure (mmHg)	Medication (daily dosage)	Time (days)	Blood pressure (mmHg)	Medication (daily dosage)	Time (months)	Blood pressure (mmHg)	Medication (daily dosage)
1	160/120	Muzolimine (30 mg) Captopril (150 mg)	7	115/80	None	38	120/70	None
2	240/130	Metoprolol (300 mg) Clonidine (0.3 mg)	8	150/90	Nifedipine (40 mg)	56	130/80	None
3	220/120	Metildopa (1000 mg) Furosemide (25 mg)	8	130/80	Labetalol (100 mg) Clortalidone (10 mg)	14	120/80	Labetalol (100 mg) Clortalidone (10 mg)
4	240/140	Hydralazine (50 mg) Nifedipine (40 mg) Clonidine (0.45 mg) Clortalidone (10 mg) Captopril (100 mg)	9	150/90	Hydralazine (50 mg) Clonidine (0.3 mg)	12	150/90	Enalapril (20 mg) Clonidine (0.45 mg) Hydralazine (25 mg)
5	180/100	Hydralazine (75 mg) Metildopa (500 mg) Clonidine (0.3 mg)	10	130/60	None	14	120/70	None
6	210/120	HCThiazine (50 mg) Nifedipine (30 mg) Oxprenolol (240 mg)	11	130/80	Nifedipine (40 mg)	40	150/80	None
7	170/115	Spirolactone (100 mg) Clonidine (0.15 mg) Hydralazine (25 mg) Captopril (75 mg)	8	120/70	Captopril (25 mg)	24	120/70	Captopril (25 mg)
8	170/130	Atenolol (100 mg) Hydralazine (50 mg)	14	140/80	Atenolol (100 mg)	66	110/80	None
9	190/120	Metildopa (1500 mg) Prazosine (3 mg)	13	150/90	None	13	150/90	Nifedipine (20 mg)
10	160/110	Clonidine (0.3 mg) Nifedipine (40 mg) Furosemide (25 mg)	9	130/80	Captopril (25 mg) Nifedipine (20 mg)	11	130/80	Captopril (25 mg) Nifedipine (20 mg)
11	190/120	Nifedipine (60 mg) Furosemide (25 mg)	8	130/80	Nifedipine (60 mg)	11	140/80	Nifedipine (20 mg)
12	220/110	Nifedipine (40 mg) Furosemide (25 mg)	8	130/60	None	11	150/90	Nifedipine (40 mg)
13	190/115	Metoprolol (300 mg) Captopril (200 mg) HCThiazine (50 mg)	8	130/90	HCThiazine (50 mg)	43	150/80	HCThiazine (50 mg)
14	195/130	Atenolol (100 mg) Nifedipine (80 mg)	10	130/60	Nifedipine (40 mg)	11	130/80	Nifedipine (40 mg)
15	190/100	Atenolol (100 mg) Nifedipine (80 mg)	8	150/90	Nifedipine (40 mg)	9	150/90	Nifedipine (40 mg)

Some side-effects were observed during the procedure: Case 9 experienced acute left ventricular failure during ethanol injection; the procedure was abandoned and successfully performed 5 months later. Case 3 developed a transient cerebral ischaemic attack 2 days after the embolization associated with a dramatic fall in blood pressure. Case 14 developed a sudden rise in blood pressure (260/140 mmHg) the day after the renal ablation, requiring treatment with intravenous sodium nitroprusside.

Discussion

Correction of lesions affecting renal perfusion is mandatory in patients with renovascular hypertension. Percutaneous renal angioplasty and reconstructive surgery are the preferred procedures. However, these techniques are not suitable for some patients because of the features of individual lesions and total nephrectomy may have to be performed. However, total nephrectomy is a high-risk procedure and cannot be carried out in patients of poor clinical status. It is in these cases that percutaneous renal ablation offers an alternative.

Therapeutic renal ablation has been performed over the last 10 years in the treatment of a variety of renal diseases. Its usefulness in renal hypertension, however, is not yet fully established, with only case reports or short series having been published (Reuter et al, 1976; Warren et al, 1982; D'Souza et al, 1984). In addition, many substances have been used to produce renal infarction and this may account for differences in reported results on blood pressure.

A long-lasting antihypertensive effect can be achieved with renal embolization only when the juxtaglomerular apparatus is totally and permanently destroyed, abolishing renin production. This can be achieved by occluding renal arterioles, but no embolizing agent has yet been shown to cause permanent vascular occlusion. In addition, some agents are technically difficult to use and others may cause abscess formation or necrosis of other organs because of back-flow from the renal vasculature (Cho et al, 1983; Nanni et al, 1983; Lammer et al, 1985).

In this study we have used absolute ethanol as the embolizing agent in all but one patient (Case 11). Ethanol has advantages in that it causes complete cellular death with total vascular occlusion, thereby eliminating the risk of vascular recanalization and activation of the renin-angiotensin system (Ellmann et al, 1980; Nanni et al, 1983; Latshaw et al, 1985). Moreover, direct injection into the aorta of experimental animals does not cause acute or delayed damage of the arterial wall and post-injection blood levels of the alcohol are undetectable (Ellmann et al, 1980, 1984). However, necrosis of gut has been reported after the injection of ethanol into kidneys with renal cell carcinoma (Cox et al, 1983). In this study we did not observe harmful side-effects due to a reflux of embolizing solution, possibly as a result of precautions used during the procedure.

For the above reasons, embolized patients have to be

carefully monitored in the days following the procedure and for many months after. In our study, therefore, the patients have been followed-up for a mean time of 24 months.

The results show that percutaneous renal ablation was successful in those patients with a long history of hypertension, suggesting that a short history is not essential for a successful outcome (Hughes et al, 1981). It is important to emphasize that the blood pressure response after percutaneous renal ablation varied considerably among our patients. In most cases, blood pressure was reduced 3–6 days after the procedure but a dramatic fall was seen within a few hours accounting for a transient cerebral ischaemic attack (Case 3) and for coronary pain (Case 5).

The results on blood pressure in this study are quite similar to those obtained after surgical treatment; in fact in 33% of our patients the blood pressure returned to normal and 66% were regarded as "improved". In a review of 1827 patients with renal hypertension, the rates of cure and improvement after surgery were 46% and 31%, respectively (MacKay et al, 1983). In addition, percutaneous renal ablation is simpler and less expensive than surgery, and can be performed in patients of high surgical risk.

In conclusion, our study shows that percutaneous renal ablation with ethanol is a safe and successful method of therapy in patients with renovascular hypertension requiring total or partial nephrectomy, and may be particularly suitable for those patients regarded as of high surgical risk. Careful clinical monitoring is required in both the short and long term.

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Central venous catheter placement for intravenous digital subtraction angiography: an assessment of technical problems and success rate

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Abstract. Scant attention has been paid to the technical aspects of central venous catheter placement in intravenous digital subtraction angiography (IV-DSA). In a prospective study of 200 unselected patients referred for IV-DSA, technical problems and success rates were recorded. Central venous access via an arm vein was achieved in 95% of patients. In 83% of cases, only one venous puncture was required. The commonest single cause for failure was being unable to find, puncture or introduce a guidewire into a suitable calibre vein at the cubital fossa in the first instance. Once entered with a guidewire, the median cubital/basilic route led to successful catheter passage to the superior vena cava (SVC) on 93% of occasions. The equivalent figure for the cephalic route was 80%. Only two out of 129 attempts at which the cephalic vein was entered failed as a result of being unable to negotiate the cephalic/axillary junction. Venous spasm and branch points in the arm were the main problems when using the cephalic vein and these together were responsible for the differences in success rate between the cephalic and basilic routes. The results indicate that in the clear majority of patients referred for IV-DSA, central venous catheter placement is straightforward. The median cubital/basilic route is preferred but even if the cephalic route has to be used, it should still provide access to the SVC in more than three-quarters of cases. Manoeuvres used to overcome access difficulties are discussed and illustrated.

Most radiologists prefer a central catheter injection to a peripheral injection in intravenous digital subtraction angiography (IV-DSA) as it is felt to give better quality images (Eskridge et al, 1983; Rubin et al, 1984; Saddekni et al, 1984). Advocates of the peripheral injection have drawn attention to difficulties and hazards in central venous catheter placement (Lea Thomas & Treweek, 1986; Doris et al, 1987). Where these technical difficulties have been discussed, however, the form has almost always been anecdotal.

The sole purpose of this study was to assess the effectiveness of central venous catheterization as a technique and to examine any difficulties that occurred.

Patients and methods

The paper is based on 200 patients referred for IV-DSA at St Mary's Hospital and all the studies were carried out by the author. The patients were unselected and every patient on whom IV-DSA was attempted has been included. The age range of the patients was 22 to 87 years with a mean of 61 years. The male to female ratio was 1.2 to 1.

A DSA set consisting of a 7-cm, 18 G, one-piece, introducer needle, a 1.5-mm J, 0.035 in, teflon-coated guidewire and a straight, 10 side hole, 5 F nylon catheter was used (William Cook Europe). The aim was to place the catheter in the superior vena cava (SVC) with its tip at the junction of the SVC and the right atrium, well away from the caval tributaries and the coronary sinus (Pinto et al, 1984).

A detailed record was made of each procedure, including note of which vein was punctured. If a guidewire could not be introduced into the vein, a little contrast medium was injected and fluoroscopy used to

ascertain why. Similarly, if the guidewire could not be advanced beyond the arm, the catheter was advanced to this point and a little contrast medium instilled to determine the cause: for example, venous spasm, branch points or valves that might snag the guide, pre-existing occlusions, or dissection during passage of the guide. With this information, every effort was made to resolve the difficulty and reach the SVC safely; if this were not possible, the initial route was abandoned and another vein chosen if available. In particular, careful note was made of any obstruction at the junction of the cephalic and axillary veins, which has been said often to prevent catheter passage to the SVC (Lea Thomas & Treweek, 1986). Any manoeuvres used to negotiate the obstruction were recorded, as was the use of any additional guidewires.

Results

Central venous catheter placement was achieved via an upper limb vein in 95% of the referred patients. In 83% of cases, only one venous puncture was required (Table I).

The commonest single cause of failure was inability to find, puncture or introduce a guide into a suitable

Table I. Success rate of central venous catheter placement

Cases successful at the first attempt	166 (83%)
Cases successful at the second attempt	20 (10%)
Cases successful at the third attempt	4 (2%)
Failed cases	10 (5%)
Total no. of cases	200

Table II. Causes of failure of catheter placement

Cause of unsuccessful attempts	Venous route used		
	Med. cub. /basilic	Cephalic	Antecubital (unspecified)
Failed puncture or guide introduction (n=20)	8	8	4
Venous spasm (n=10)	2	8	—
Unnegotiable branch point (n=6)	0	6	—
Pre-existing occlusion (n=10)	4	6	—
Dissection (n=4)	0	4	—
Unnegotiable cephalic/axillary junction (n=2)	N/A	2	—

N/A = not applicable; Med. cub. = median cubital.

calibre vein in the first instance (Table II). A guide, once introduced into a vein, led to successful passage to the SVC in 93% of attempts using the basilic route and in 80% of attempts using the cephalic route (Table III). Attempted catheterization using the cephalic route was therefore more troublesome, but the difference was due to venous spasm and branch points in the former, rather than difficulty at the cephalic/axillary junction. Failure to pass this point occurred only twice in 129 attempts at which the cephalic vein was entered.

The chosen vein was dissected on four separate occasions; all involved the cephalic vein, all occurred in the arm and all were associated with venous spasm. There were no cases of mediastinal dissection, perforation or extravasation.

Discussion

There has been no previous study devoted to the technical difficulties and success rate of central venous catheter placement, although Popky et al (1984) showed that peripheral cannulation was quicker than central catheterization, and in a large series, Pinto et al (1984) reported 13 cases where upper limb venous puncture failed and the femoral route had to be used.

Table III. Success rate of passage of guidewire to the superior vena cava

Vein used	Number of occasions	Number successful	Percentage successful
Cephalic	137 (129)	103	75 (80)
Median cubital/basilic	99 (91)	85	86 (93)
Antecubital (unspecified)	4 (0)	0	0

The figures in parentheses are derived by subtracting the number of occasions where the vein was never entered with a guidewire in the first instance.

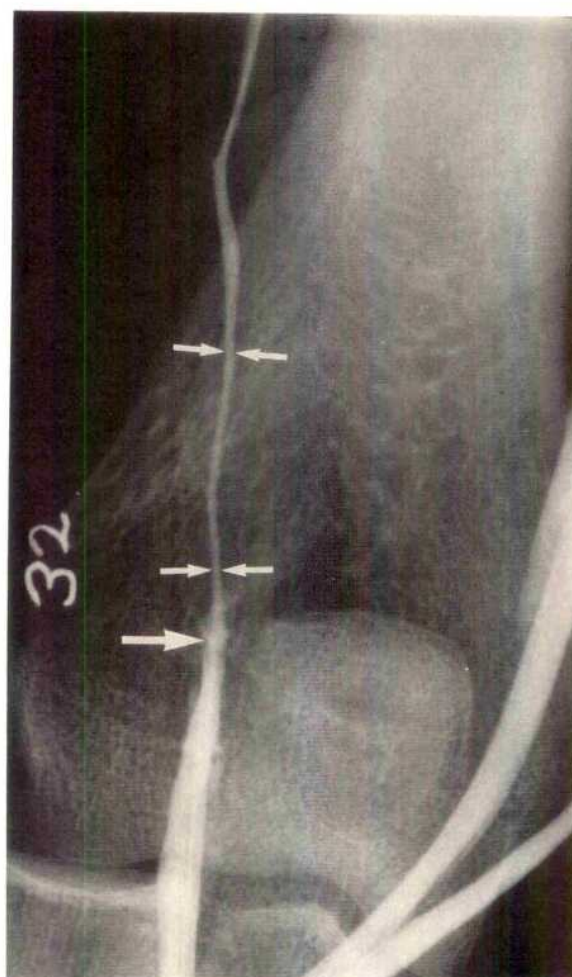


Figure 1. This cephalic vein was cleanly entered with a needle. The J guidewire would not advance. Contrast medium revealed marked spasm (small arrows) proximal to the needle tip (large arrow). The straight end of the guidewire and then the catheter passed proximally without difficulty.

It is generally assumed that the basilic vein is the preferred route because of its continuity with the axillary and subclavian veins and these results confirm this. The basilic vein itself, however, is postero-medial at the elbow, so not easily approached, and its mobility also makes puncture more difficult. The median cubital vein is ideal inasmuch as it lies directly anterior at the cubital fossa, is fairly well supported and of course runs superomedially to join the basilic vein. Unfortunately, in a few instances the median cubital vein is absent and in many more it is a small calibre vein, or is only evident on palpation. The cephalic is usually the largest and best supported vein at the cubital fossa but with the drawback that once entered, there are more problems than with the basilic. If there is a reasonably good-calibre median cubital vein visible or palpable, it should be the first choice of puncture site.

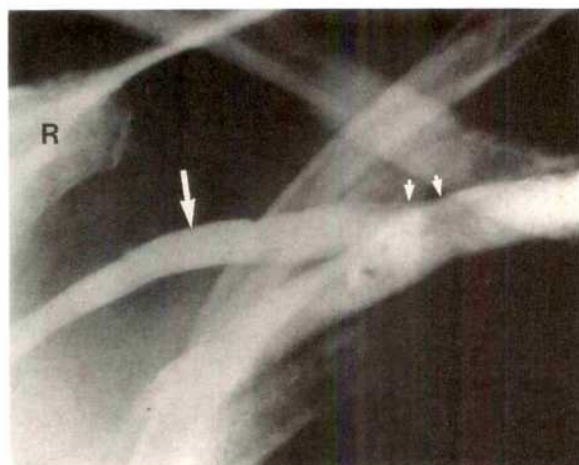


Figure 2. Both the first bend (large arrow) and the cephalic insertion at the axillary (small arrows) are shallow and were easily passed.

Venous spasm in the arm was a very real entity in the cephalic vein (Fig. 1). In eight cases, it prevented advancement of the catheter and all four cases of dissection were preceded by spasm. Once recognized, it was usually negotiated simply by using the straight end of the guidewire as far as the shoulder, advancing the catheter to this point and then re-introducing the J end. There was the definite suspicion that the J configuration exacerbated spasm in the arm, and may even have been the initiating factor. The J guidewire is, however, considered essential more proximally to avoid perforation or dissection.

The cephalic vein turns inferiorly to pass through the clavipectoral fascia and insert into the axillary vein. The angle of the first bend and that of the insertion vary considerably. Both may be shallow and present no difficulty at all to the passage of the guidewire and

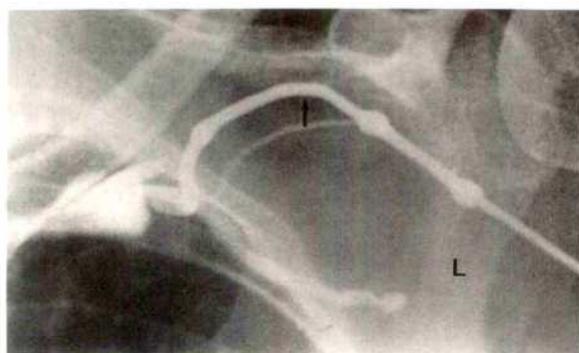
catheter (Fig. 2). Not uncommonly, the first bend approximates to a right angle and may thus cause hold-up of the guidewire. This is easily dealt with by abducting the arm, which straightens the bend and allows the J guidewire through (Fig. 3). Crossing the junction of the cephalic and axillary veins is very rarely a problem. The guidewire, once in the axillary vein, may favour turning distally towards the arm, but one or two further careful attempts have always seen it pass proximally into the subclavian; often, full fixed inspiration permits this to happen, presumably by subtly altering the configuration of the junction.

Mediastinal extravasation has been reported using straight catheters and attributed to catheter recoil and jamming of the tip in a caval tributary (Rosen et al, 1983; Pinto et al, 1984). Each of these authors experienced two such cases, following which they modified their technique to include a linear rate rise of 0.3 s on the power injector. Pinto et al (1984) also stressed the importance of using a 10 side hole catheter, the tip of which should be placed well away from venous tributaries. Following these modifications (and still using a straight catheter) Rosen et al (1983) did not have a single case of extravasation in the next 500 studies and Pinto et al (1984) had none in the next 1700.

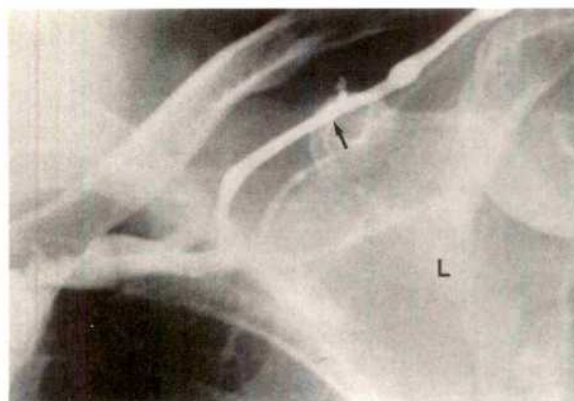
Pigtail catheters are said to minimize extravasation risks and are recommended by Saddekni et al (1984), although there is no mention of catheterization success rate. Others have found them both difficult and painful to insert and remove (Rosen et al, 1983; Pinto et al, 1984).

Conclusion

In the clear majority of patients, central venous catheter placement for IV-DSA can be carried out with neither difficulty nor hazard. Previous accounts of difficulty with this technique should not be allowed to influence one unduly against a central venous injection site for IV-DSA.



(a)



(b)

Figure 3. (a) The configuration of the first bend with the arm by the side. (b) The configuration with the arm abducted. Note the bend is now straightened.

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Fetal fat measurement by magnetic resonance imaging

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Abstract. A method to assess the average percentage of fetal fat with respect to other fetal tissue is described. This method was then used to assess the percentage of fat in 13 normal fetuses who had a magnetic resonance imaging (MRI) examination late in pregnancy (38-41 weeks). The scans of a further 13 fetuses of diabetic mothers and one case of intrauterine growth retardation (IUGR), all of whom had MRI examinations in the last 3 years, were reviewed and similar calculations were carried out. Whilst the percentage fat range in the normal group was large, it was still possible to discern a difference between the normal, diabetic and IUGR cases.

The potential of magnetic resonance imaging (MRI) in the study of the human fetus has long been recognized with the obvious advantages of the lack of ionizing radiation exposure of mother and fetus, the absence of bone artefact from the maternal pelvis and the unique ability to image fetal morphology and body composition (Smith et al, 1983, 1984, 1985; Smith, 1985).

The results of a preliminary study on 13 women with normal pregnancies, comparing the ability of ultrasound and MRI to assess fetal fat thickness, showed that while ultrasound proved accurate, the MRI values were less so. Reasons for the failure of MRI included the limited accuracy of measuring distances of 3-5 mm on a system where there are only three pixels to 1 mm. Skinfold caliper and ultrasound measurements of subcutaneous fat give an indirect measure of total body fat and may be prone to error because of differences in focal fat distribution. The most accurate method of assessing total body fat is by underwater weighing, but since this is not possible when studying neonates, the potential of MRI to do this has been exploited. Because the MRI signal from fat is characteristic, it is possible to calculate the amount of fat, both subcutaneous and intra-abdominal, by making use of specific T_1 measurements of fat and other tissues. It was therefore decided to modify a technique developed in Aberdeen for measuring adult total body fat for the assessment of fetal fat (Hayes et al, 1988). To this end we have devised a means of obtaining an average total fetal fat value expressed as a percentage of total fetal tissue.

Method

Thirteen women in the late stages of normal pregnancy had an abdominal MRI examination performed; gestation varied between 38 and 41 weeks.

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Magnetic resonance imaging was carried out using the Aberdeen Mark II four-coil, 0.08 T, air-cored, resistive, vertical field magnet for which the resultant resonant frequency for hydrogen protons is 3.4 MHz (Redpath et al, 1987). A midline, sagittal section was obtained with the patient lying supine to assess fetal lie and placental site, followed by a series of axial sections of 16 mm thickness, 20 mm apart, over the length of the uterus with the patient lying on her side, or in whichever position was most comfortable. A pulse sequence designed by Edelstein and Hutchison was used (Edelstein et al, 1980; Hutchison et al, 1980). This pulse sequence consists of readout pulses every 1000 ms with alternate pulses being preceded by adiabatic fast passage (AFP) with a constant delay of 200 ms between the readout pulse and the AFP. In other words, the pulse sequence consists of interleaved saturation-recovery (SR) (S_1) and inversion-recovery (IR) (S_2) pulses (recovery time (TR)=1000 ms, inversion time (TI)=200 ms). After acquisition, the data were displayed as SR and calculated T_1 images on a grey scale visual display unit (Fig.1). When calculated T_1 images were used, T_1 was calculated for each pixel from the formula:

$$T_1 = 200 / \ln (2 \times S_1 / (S_1 - S_2))$$

The acquisition time for each section was 4 min 15 s.

A series of 120 T_1 values of fetal fat were obtained from these scans and over 90% of these values fell within the range 180-240 ms (maternal buttock fat had a range of 140-150 ms). Values above 240 ms were discarded as it was felt they might overlap the T_1 values of other fetal tissues. To calculate the fat content of a fetus, the individual sections of a scan were studied using an image display system (IDS) developed in the Department of Bio-Medical Physics and Bio-Engineering of the University of Aberdeen; the Department's DEC VAX 11/750 computer was run using SIGMEX ARGS 7000 image display hardware. A region of interest was drawn around the amniotic sac

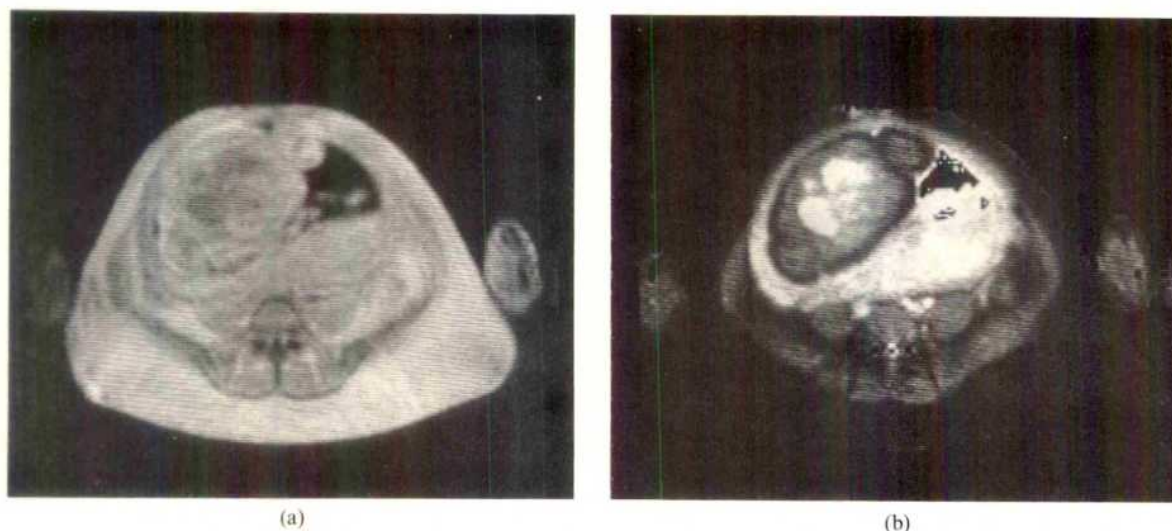


Figure 1. (a) Saturation-recovery and (b) calculated T_1 images.

using a tracker ball to guide a cursor round the image displayed on the monitor screen. The image display system allows the choice of four images: SR, a T_1 -weighted image, IR and calculated T_1 , on which to draw the region.

It was found that the SR and T_1 -weighted images were most used as they gave the clearest outline of the amniotic sac. A frequency distribution of the T_1 values in the region was then transferred to disk for further analysis. This distribution gives the number of pixels in the region with T_1 values of 0–1030 ms. As each pixel could be related to a fixed volume of the fetus, an estimation of fat content can be made by finding the proportion of pixels with T_1 values in a range taken to identify fetal fat. The amniotic fluid with its high T_1 value of over 1000 ms was eliminated from the calculation so that, in effect, only fetal tissue was considered. Using the T_1 range of 180–240 ms for fetal

fat, the proportion of fat was calculated for each slice. An approximation to the proportion of fat in the fetus was found by taking the proportion over all the slices. This process was repeated for each of the 13 fetuses examined.

The babies were examined by one observer within 48 h of birth and their birth weight, crown–heel measurements and, in 11 cases, skinfold thickness of triceps, mid-thigh and subscapular region of the back were taken using skinfold calipers (Oakley et al, 1977). Having studied this group of 13 normal pregnancies, MRI examinations that had been carried out over the last 3 years on fetuses of mothers with poorly controlled diabetes (12 insulin dependent, one gestational diabetic) in their late pregnancies were reviewed and the same calculations performed. Similarly, an examination of one case of an intrauterine growth retarded (IUGR) fetus of a non-diabetic woman (K.P.) was reviewed.

Table 1. Details of the fetuses of the group of normal pregnancies in non-diabetic women

Patient	Gestation at time of scan (weeks)	Gestation at time of birth (weeks)	Birth weight (g)	Total average % of fetal fat
L.D.	40	42	2940	14.6
K.S.	38	40	2950	21.4
F.S.	41	41	3160	14.3
A.G.	40	41	3250	21.3
C.T.	40	40	3330	18.4
I.I.	40	42	3410	16.3
A.S.	40	40	3430	12.3
P.B.	38	41	3500	12.6
G.M.	40	40	3630	18.4
D.S.	41	42	3700	11.8
J.W.	40	41	3730	25.0
A.G.	41	42	3950	18.1
J.A.	41	42	4300	18.5

Table II. Post-natal skinfold values obtained on 11 babies of the group of normal pregnancies of non-diabetic women studies compared with total percentage body fat as measured by MRI

Patient	Total average % of fetal fat measured by MRI	Skinfold thickness (mm)		
		Triceps	Mid-thigh	Back
A.S.	12.3	3.7	5.0	5.0
P.B.	12.6	4.4	4.6	4.4
F.S.	14.3	4.4	5.5	4.9
L.D.	14.6	4.0	4.6	4.0
I.I.	16.3	6.0	7.2	5.4
A.G.	18.1	4.4	5.6	4.8
C.T.	18.4	5.4	5.4	4.8
G.M.	18.4	5.0	5.6	4.5
L.A.	21.3	4.2	4.8	4.2
A.G.	21.3	4.6	4.1	4.6
K.S.	21.4	4.8	5.0	5.0

Results

Table I shows the values of the total average percentage of fetal fat per patient obtained by analysing every axial section that demonstrated a recognizable amniotic sac containing fetal tissue. If the highest and lowest sections contained only a small or ill defined area of sac, or very little fetal tissue, these sections were excluded from the calculation.

The total average percentage of fat per fetus was 17.2% (range 11.8–25%). Average birth weight was 3483 g (range 2940–4300 g) and all babies lay between the 10th and 90th centiles for weight/gestation. Skinfold thickness over triceps, mid-thigh and subscapular area of the back were measured within 48 h of delivery on 11 of the babies (Table II). Apart from one triceps measurement of 3.7 mm (A.S.) and one mid-thigh measurement of 7.2 mm (I.I.), all values lay between 4.0 and 6.0 mm. Seven babies had their subcutaneous fat thickness checked using a 7.5 MHz ultrasound transducer and these results showed close correlation with the skin caliper values. Correlation between ultrasound and MRI was not possible because of the

large size (1 mm²) of the cursor used to measure MRI fat thickness.

Table III shows the results obtained on the babies of poorly controlled diabetic mothers, 12 of whom were long-standing insulin-dependent diabetics; one (J.P.) was a gestational diabetic. Average birth weight was higher than the normal group, as would be expected, at 3872 g (range 2840–5450 g) and the total average percentage of fat per fetus was also higher at 27.4% (range 15.6–33.6%). Only three fetuses (H.J., M.Y., A.B.) had a percentage of fat lower than 25%, *i.e.* the highest value obtained from the normal group. All but four babies lay within the 10th–90th centiles for weight/gestation; three (J.P., A.B., M.D.) were above the 90th centile and these had percentage fat values of 30.1, 23.8 and 31.1%, respectively. One baby (H.J.) lay below the 10th centile and the percentage fat calculated in this case was 15.6%. Since this was a retrospective study, skinfold thickness measurements were not possible in the diabetic patients.

In the case of the single IUGR baby (K.P.), the average percentage fat value at 38 weeks was 3.6%. The

Table III. Details of the fetuses of the group of diabetic women studied

Patient	Gestation at time of scan (weeks)	Gestation at time of birth (weeks)	Birth weight (g)	Total average % of fetal fat
H.J.	39	40	2840	15.6
G.D.	38	40	2940	26.8
D.M.	38	39	2990	30.8
J.R.	38	39	3480	26.3
K.M.	38	41	3520	30.6
E.H.	39	40	3540	31.5
Y.B.	38	40	3600	33.6
S.M.	38	38	3830	28.4
F.U.	38	40	4870	25.5
M.Y.	38	40	4100	22.9
A.B.	37	38	4300	23.8
J.P.	37	40	4870	30.1
M.D.	37	39	5450	31.1

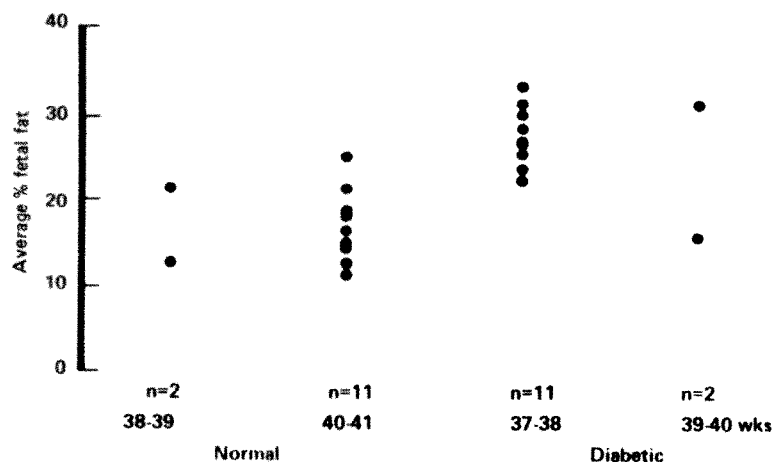


Figure 2. Average percentage of fat in normal and diabetic babies who had MRI examinations performed between 37 and 40 weeks gestation.

baby was delivered at 39 weeks gestation and its birth weight was 2600 g.

Discussion

The 13 babies studied initially (Table I) all lay within the 10th–90th centiles on sex-adjusted weight/gestation tables. The skinfold thickness values measured by skinfold calipers (Table II) lay within a small range and the accuracy of these measurements was substantiated where possible by ultrasound. The apparent poor correlation between the percentage fat measured by MRI and the skinfold caliper measurements reflects the inability of skinfold measurements to assess intra-abdominal fat, suggesting that MRI is a more complete method for assessing body composition. No baby experienced post-delivery problems necessitating medical treatment during their stay in hospital. We were therefore satisfied that a group of normal fetuses had been studied.

The values obtained for percentage of fetal fat by this method are by no means absolute, but by studying these normal babies, a reference group has been obtained against which other potentially abnormal fetuses can be compared. The average percentage of fat per fetus was 17.2% (Widdowson (1981) quotes an average fetal fat value of 15% in a full-term 3.5 kg baby). The range of fat percentage was large (11.8–25%), but nevertheless it was possible to show distinct differences between these babies, those of the poorly controlled diabetic mothers (Fig. 2) and the single case of IUGR.

Almost all of the values for the diabetic group lay above the normal range. The method proved successful in distinguishing the one case (H.J.) that lay below the 10th centile and, whilst the percentage of fat in this baby was within the normal range group, it was well below that of the diabetic group. This group of 13 comprised patients with poorly controlled diabetes and was chosen because we expected to see significant differences in fetal fat compared with normal pregnancy.

No attempt was made to establish a direct relationship between body weight and percentage fat in

either of the groups, nor have we distinguished between the stages and degree of control of the diabetic mothers.

It is hoped that another area of potential for this method will be the ability to distinguish small babies suffering from IUGR from babies who are small, but otherwise normal. This distinction is not always easy to make clinically or with ultrasound and would prove extremely useful to the obstetrician with regard to patient management in the last weeks of pregnancy. At present, only single measurements in late pregnancy have been obtained. As it would be an advantage to identify at-risk babies earlier than 38–40 weeks, serial studies of normal pregnancies from 30 to 40 weeks are being undertaken in order to compile growth curves with which to compare single or serial studies of abnormal pregnancies. Comparison of fetal growth in twin pregnancy is another potential area of application for this regime.

As the range of T_1 values can be readily altered to consider other tissues, e.g. amniotic fluid, this method could be used to quantify amniotic fluid and assess abnormal changes in intrauterine fluid volume. It is felt that this is a valid and acceptable way to consider fetal growth in the last trimester of pregnancy and one that may prove useful to the obstetrician in the management of certain patient groups.

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Use of a radon mould technique for skin cancer: results from the Peter MacCallum Cancer Institute (1975–1984)

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Abstract. During the period from 1975 to 1984, 642 patients had non-melanoma skin cancers (NMSC) treated by a radon mould technique following the principles of the Manchester system. The results of 77 out of 642 (12%) with histologically verified lesions are presented. The sites of the lesions were as follows: head and neck 25 (32%), upper limbs 38 (49%), lower limbs 13 (17%) and trunk one case only. The histological diagnosis was squamous cell carcinoma 48 (62%), basal cell carcinoma in 22 (29%) and other in seven (9%). There were nine out of 77 (12%) failures, four with persistent disease, which did not clear after initial treatment (and for whom the radon mould was an inappropriate choice of technique), and five (6%) recurrences after clearance of the initial lesion. There was a sharp rise in failures after 1979 when there was a change of radon supplier, but no calibration error was substantiated. It is clearly beneficial for institutions to cross-check the manufacturer's brachytherapy source data. There have been no further recurrences or any symptomatic late morbidity. This is a safe, effective and practical radiotherapeutic technique for superficial lesions (not exceeding a depth of 4 mm) in areas of poor radiation tolerance, and may obviate the need for a prolonged fractionated course of external-beam radiation in selected patients. Alternatives to radon are discussed.

The treatment of surface lesions by the direct application of radioactive sources has been practised since the earliest days of radiotherapy. The Manchester system of mould technique and dose prescription has been widely accepted and has stood the test of time (Paterson & Parker, 1947). Whilst still adhering to the Manchester system, the radioactive material used in the moulds may be changed from radium to other suitable γ -emitting radionuclides, e.g. radon, gold, caesium, cobalt. At the Peter MacCallum Cancer Institute (PMCI), radon has been used because of the convenience of ready availability in any desired activity and length of capillary. The short half-life enables many treatments to be done on an outpatient basis.

In the period from 1975 to 1984, 642 patients had skin lesions treated by a radon mould technique following the principles of the Manchester system. Details of the technique are presented along with the results achieved in 77 out of 642 (12%) patients in whom there was a biopsy-proven diagnosis of non-melanoma skin cancer (NMSC).

Materials and methods

Description of the technique of superficial radon mould treatment

The radiotherapist marks the volume to be treated and an impression of the area is taken. Patients seen at the Melbourne city clinic have an impression taken with wax, which is cut to the required size (5 mm larger than

the radon area all round) and treatment height h , and then softened in warm water (60°C). The softened wax is then easily moulded over the area, with care being taken not to decrease the treatment height. The moulded wax is then cooled in water and this impression is now used for the radon mould. Grooves for the radon sources are scratched on the mould surface sufficiently deeply for h to equal the distance from the skin to the centre of the source. Heated wax is gently deposited over the sources from the end of a knife to keep them in place. The completed mould is shown in Fig. 1. At the next visit the mould is fitted to the treatment area and is secured by an Elastoplast (zinc oxide) bandage or micropore tape in patients with zinc oxide skin allergic history (Fig. 2). Patients seen at country clinics have a plaster of Paris bandage impression made of the area and a wax mould is made from this in Melbourne. This is fitted to the patient at the next visit to the country clinic. Patients requiring moulds of an activity greater than 600 MBq are admitted to hospital and treated in a side-ward. The complete treatment may be given as an inpatient if this is felt to be more practical, but most patients either have the whole treatment at home or complete it there after decay of the radon to less than 600 MBq. The patient returns to the clinic to have the mould removed (Fig. 3). The standardized overall treatment time was 6 days and 20 h.

At PMCI the moulds are constructed from lengths of gold capillary containing radon. These are placed on the wax mould in accordance with the Paterson–Parker rules. Radon has a half-life of 3.83 days with a γ -ray energy range of 0.61 to 2.09 MeV. One initial millicurie of radon decaying for infinite time is equivalent to 132.4 mCi h of radium. The number of millicurie hours

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Figure 1. Illustration of two moulds showing the source arrangement.

required per 10 Gy of dose prescribed for a fixed time are obtained from standard tables and graphs. The tumour dose is usually fixed at 40 Gy and the depth at which the dose should be delivered is specified by the radiotherapist according to the estimated depth of the lesion, and hence usually only the skin dose is varied.

Radiation safety precautions

Radon in gold capillary tubing is supplied in the specified lengths and strengths cut to order for the construction of each individual mould. The mould room technician works behind a thick lead screen and uses long-handled forceps to transfer the radon from the shielded container onto the pre-marked positions on the mould and to secure them with a spot of molten wax. The loaded mould is then applied to the patient and secured in position with adhesive tape. At removal, the activity has decayed to nearly one-quarter of that at application. The mould is stored for a further 1–2 months before dismantling and returning the gold capillary to the supplier for re-use. Loading, applying the mould and removal takes of the order of 3 min and exposure of the staff both to the whole body and to extremities is minimal.

The conditions under which patients may be discharged for completion of their treatment at home are set by the National Authority based on the recommendations of the International Commission on Radiological Protection. The patient is given both verbal and detailed written instructions to avoid close contact with other members of the household, especially children, young people and pregnant women. Information is provided on the necessity for minimal handling of the applicator consistent with comfort and hygiene and an emergency contact given in case the mould becomes dislodged.

For country patients, arrangements are made for the mould to be removed on the next visiting clinic day if this coincides with the completion of treatment. Alternatively, the patient is instructed to remove the mould and an appropriate storage box is provided for later return to the main hospital. If the patient is to be



Figure 2. Mould *in situ* under a bandage on the patient's leg.

admitted to hospital then the usual nursing precautions for radioactive patients apply.

Results

Patients

The biopsy-proven patients consisted of 47 males and 30 females, a male to female ratio of 1.6 : 1. The mean age at the time of treatment was 72 years with a range of 37–98 years. The sites of the lesions were head and neck 25 (32%), upper limbs 38 (49%), lower limbs 13 (17%) and trunk 1 (1%). Details are set out in Table I.

Tumour and treatment details

The histological diagnosis was as follows: squamous cell carcinoma (SCC) in 48 out of 77 cases (62%, well differentiated SCC in 21 and moderately differentiated in four cases), basal cell carcinoma (BCC) in 22 out of 77 (29%), baso-squamous in three out of 77 (4%), Bowen's disease with invasive features in three out of 77 (4%) and keratoacanthoma in one (1%). The lesions treated varied from 4 mm × 4 mm × 1 mm (16 mm³) to 45 mm × 35 mm × 4 mm (6300 mm³) with a median

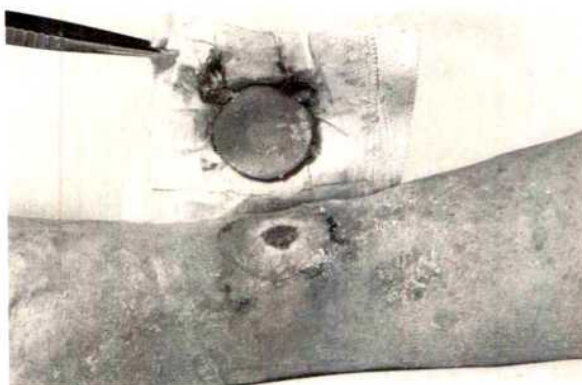


Figure 3. Mould and bandage being removed, showing the tumour area.

Table I. Sites of lesions

	Male	Female	Number	%
Head and neck (25–32%)				
Scalp	12	1	13	17
Forehead	5	5	10	13
Temple	2	0	2	3
Upper limbs (38–49%)				
Shoulder	1	0	1	1
Upper arm	1	0	1	1
Forearm	2	5	7	10
Wrist	1	1	2	3
Dorsum of hand	16	10	26	34
Palmar aspect thumb	1	0	1	1
Trunk (1%)				
Chest (over sternum)	0	1	1	1
Lower limbs (13–17%)				
Lower leg	5	6	11	14
Foot	1	1	2	3
Total	47	30	77	

volume of 1099 mm³. To express tumour bulk, the volume was determined from the estimated rectilinear dimensions. Activity of radon used varied from 203 to 1107 MBq.

The depths at which the tumour doses were prescribed ranged from 1 to 4 mm. The tumour dose prescribed was 40 Gy in 75 cases (35 Gy and 36 Gy in one case each). The skin dose thus varied from 47 to 62 Gy, but usually did not exceed 55 Gy.

Table III. Failures by year of treatment

Year	Number of lesions treated	Persistent lesion	Recurrent lesion	Overall failure
1975	14	0	0	0
1976	13	0	1	1
1977	22	0	0	0
1978	5	0	0	0
1979	5	2	1	3
1980	4	0	1	1
1981	5	0	0	0
1982	4	0	1	1
1983	4	2	1	3
1984	1	0	0	0
Total	77	4	5	9

Treatment results

Sixty-two (80%) patients were followed-up for more than 12 months and the median follow-up time was 45.3 months (range 1–146 months). Four patients had persistent disease after treatment and required other measures to ablate the lesions at 3–7 months after initial therapy. There were five recurrences 6–66 months after treatment. This gives an overall failure rate of nine out of 77 cases (12%). Failures are analysed in Table II.

Treatment failures are also set out by year in Table III. It can be seen that the failure rate in 1975–1978 was one out of 54 (2%) and from 1979 to 1984, eight out of 23 (35%). This marked change in failure rate occurred

Table II. Persistent lesions (four cases) and recurrent lesions (five cases)

	Year	Histology	Site	Lesion volume (mm ³)	Dose and depth treated	Skin dose (Gy)	Activity (MBq)	Treatment and when
Persistent lesions	1979	SCC	Lower leg	1000 (20 × 25 × 2)	35 Gy at 2 mm	48	273 h=0.5	Surgery 5 months
	1979	SCC	Dorsum of hand	6160* (45 × 35 × 4)	40 Gy at 4 mm	56	1107 h=1	7 MeV electrons 7 months
	1983	SCC	Scalp	1120 (16 × 14 × 5)	40 Gy at 3 mm	54	654 h=1	Surgery 4 months
	1983	SCC	Forehead	2100 (35 × 30 × 2)	40 Gy at 2 mm	48	736 h=1	7 MeV electrons 3 months
Recurrent lesions	1976	BCC	Upper arm	70 (7 × 5 × 2)	40 Gy at 2 mm	54	298 h=0.5	Surgery 29 months
	1979	Baso-squamous carcinoma	Scalp	864 (21 × 20 × 2)	40 Gy at 2 mm	54	322 h=0.5	Surgery 7 months
	1980	BCC	Forehead	3750 (50 × 25 × 3)	40 Gy at 3 mm	59	797 h=0.5	Surgery 66 months
	1982	SCC	Dorsum of hand	600 (20 × 15 × 2)	40 Gy at 2 mm	54	370 h=0.5	Surgery 10 months
	1983	SCC	Scalp	462 (14 × 11 × 3)	40 Gy at 3 mm	56	659 h=1	Surgery 6 months

*Fixed to muscle—amputation.

in 1979, which was the year the radon source suppliers were changed. The reason for this change in results might be explained by differences in calibration, resulting in an underdosage of the cases treated after 1979, but investigation has failed to substantiate this.

Eight of the nine failures were successfully salvaged by either surgery (seven cases) or re-irradiation (two cases), but one of the persistent lesions required limb amputation and the patient subsequently died of metastatic disease.

Discussion

Despite the widespread use of mould techniques, published reports of experience and results achieved in the management of skin cancer are unusual. The main indication for use of this technique in skin cancer is to treat superficial lesions at sites of poor radiation tolerance such as the dorsum of the hand and the anterior lower leg, particularly in elderly people where the skin is often thin and healing after radiotherapy is poor.

Theoretically, the percentage depth-dose profile that results from mould application minimizes the dose to bone and subcutaneous tissues, which would be higher with superficial X-ray or electron beam treatments. Continuous low-dose-rate irradiation is also thought to spare normal tissues. A specific advantage of radioactive moulds compared with superficial X rays is the reduced absorption in bone relative to that in soft tissue. This is significant when superficial lesions lie in soft tissues overlying bone, *e.g.* on the arm, especially the back of the hand, on the lower leg and on the head, especially the temporal region. In this series no chronic radionecrotic ulcers were produced as a result of mould treatment. The acute reaction is usually brisk and may last for several weeks. Elevation of the limb and the prevention and treatment of infection is required in all cases until the acute reaction has settled. There is a logistic advantage in being able to treat such lesions in a short overall time, whereas a protracted fractionated course of external-beam irradiation would be required at sites of poor radiation tolerance to minimize the incidence of radionecrosis. Unless poor home support or compliance or a high activity make hospitalization necessary, most treatments can be done on an outpatient basis.

There are several radioactive nuclides such as gold 198, radon 222, iridium 192, cobalt 60 and caesium 137 that may be used in moulds for brachytherapy. The short-lived materials, gold 198 and radon 222, are suitable for single-use, special-purpose applications and may be used on an outpatient basis. Use of the longer-lived materials requires the patient to be admitted to hospital for the entire treatment period.

Radon 222 has been readily available in this country for many years at a modest cost and is the material of choice in this Institute. We do not specifically advocate the use of radon, and indeed it seems likely that it will cease to be available to the Peter MacCallum Cancer

Institute in the near future, and a change will be required, probably to gold 198.

The dose of 40 Gy prescribed at depth (with a skin dose varying from 47 to 62 Gy, but usually not exceeding 55 Gy) may appear to be low at first sight. However, it has long been accepted in Australian practice that homogeneous tumour doses of 60 Gy or their equivalent are unnecessary to cure small NMSCs. The predominant use of non-standard (*i.e.* 2 Gy) fractionation in the treatment of NMSC, together with variations in end-point definition for local failure and necrosis, render comparison difficult. No other published series for mould treatment of skin cancer have been identified in the literature, and comparison has only been possible with results achieved using superficial X-ray therapy (SXRT). The 12% failure rate is high for NMSC treatment at this and other institutions (Ashby *et al*, 1989). However, it is clear that four of these cases should not have been managed by this technique (Table II). Large, bulky lesions and those whose thickness exceeds 4 mm should not be treated by radon mould application and if these cases are excluded the failure rate drops to 6%. This compares more favourably to recurrence and 5-year failure-free survival rates of 3.7% and 90%, respectively, reported from this Institute in the treatment of NMSC by SXRT (Ashby *et al*, 1989).

The increase in failure rate that occurred after 1979 when the source suppliers changed has been investigated. Underdosage owing to calibration changes has not been substantiated. There has been no upward revision of doses prescribed at depth. This further reinforces our belief that institutions should cross-check all the manufacturer's data on brachytherapy sources. A close watch is being maintained on recurrence and necrosis rates, and stricter selection criteria of lesions treated are being applied since these findings. It is noted, however, that all four lesions considered to have been inappropriately selected for the technique were included in the post-1979 group of failures, and this may have artificially increased the failure rate in this time period.

The practice of treatment of large numbers of unbiopsied skin lesions has now ceased. The cases analysed in this series represent only the biopsy-proven lesions: 12% of the 642 radon mould treatments performed in the period 1975–1984. The number of moulds performed each year has steadily declined in the context of decreasing numbers of patients with skin cancer being treated by radiotherapy at this and another large Australian centre (Kearsley *et al*, 1987; Ashby *et al*, 1989). The high degree of selection of patients for this technique is demonstrated by the fact that only 642 cases were treated in a skin clinic seeing up to 2000 new cases per annum.

The radon mould technique developed and used over many years at this Institute is a safe, effective and practical radiotherapeutic technique for superficial lesions (not exceeding a depth of 4 mm). In areas of poor radiation tolerance, it may obviate the need for a prolonged fractionated course of external-beam

irradiation in selected patients. It is also useful in situations where surgery presents difficulties, owing to site, tumour extent or general medical fitness.

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Microcomputer processing of film radiographs

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Abstract. An inexpensive image processing system, assembled from commercially available components and driven by "in-house" software, was tested as a means of processing radiographs obtained in a radiology department. In this preliminary study, the main interest was to investigate, through subjective appraisal, the ability of the system to recover the image quality of poorly exposed radiographs. Subsidiary objectives were to obtain some information regarding the specification limits of the system and its components, as well as some quantitative estimate of its advantages for clinical diagnosis. The system was used to process a set of film radiographs of an anthropomorphic chest phantom, produced under conditions that were designed to provide a wide range of image qualities. Following this, four sets of randomly ordered processed and unprocessed images were formally assessed by a group of experienced observers. Consensus opinion from the group indicated that significant improvement could be obtained through simple image processing. Some radiographs regarded as unacceptable became, after processing, acceptable to viewers.

Microcomputer technology has reached the stage where it can provide the basis of an entry-level system for digitizing, processing and displaying radiographic images. Software-driven microcomputers are slower than hardwired systems and have smaller memories than minicomputers, but they are adequate for many purposes, including dual-energy subtraction (Speller et al, 1983) and single-image processing of film radiographs (Selzer, 1984; Smathers & Brody, 1985). Because they represent a relatively small capital investment and are easily upgraded, they could have many applications in the digital radiology department (Moore & Eddleston, 1985).

A standard microcomputer system can produce digitized radiographs with up to 1024 by 768 pixels and as many as 256 grey scales. The resolution is approximately 2 line pairs per mm and inferior to that of a low-sensitivity film-screen combination, which can resolve 10 line pairs per mm at about 10% modulation transfer function (MTF) (International Commission on Radiation Units and Measurements (ICRU), 1986), and the 5 line pairs per mm that is typical of a digital fluoroscopy system (Giger & Doi, 1985). Without some process of zooming and scanning, the system is not able to offer much diagnostic assistance in the spatial dimension, but, in the contrast dimension, the situation is more promising, since the digitizing system may be capable of measuring more grey scales than can be distinguished directly by an observer. In principle, 256 grey scales are readily achieved, but, in practice, this threshold contrast may be increased considerably by noise effects. Numerous studies have been made of noise sources and their effects on contrast visibility in digital radiography systems (Cohen et al, 1981; Shaw & Bessano, 1982; Giger & Doi, 1984; Harrison & Kotre, 1986). In general, the major source of noise in a microcomputer digitizing system is likely to be the television camera, which, with a 40 dB signal-to-noise ratio (SNR), should support about 100 grey scales.

For these reasons, the present study has been concerned with the contrast enhancement of single digitized film radiographs. The specific objective has been to determine the extent to which such processing may be able to recover incorrectly exposed radiographs, that is, to render acceptable a number of radiographs that would otherwise be regarded as of unacceptable quality.

The radiographs

A commercially available anthropomorphic chest phantom, of the type commonly used for radiographic training, was used as the subject for the radiographs in this study. The foundation of the phantom is the thoracic section of a human skeleton. The chest cavity and surrounding body is composed of suitable tissue substitute materials. In the production of the lung substitute sections, the manufacturer has made no attempt to simulate bronchial or other details.

A controlled set of radiographs of the phantom was produced in the X-ray Department of Charing Cross Hospital, using the department's current general-purpose film-screen combination. As a preliminary exercise, the X-ray equipment was assessed for kilovoltage accuracy and exposure linearity over all of the ranges employed in the radiography. By maintaining constant exposure geometry, all of the images produced were spatially identical.

The structure of the set of radiographs is a 3 by 3 matrix in which radiographic exposure and kilovoltage are varied along the rows and columns, respectively, and in which the central element is considered to be an ideal radiograph. Accordingly, the array, which is shown in Fig. 1, represents a controlled group in which image quality is systematically varied.

The processing system

The components of the image acquisition and processing system are a standard illuminated viewing

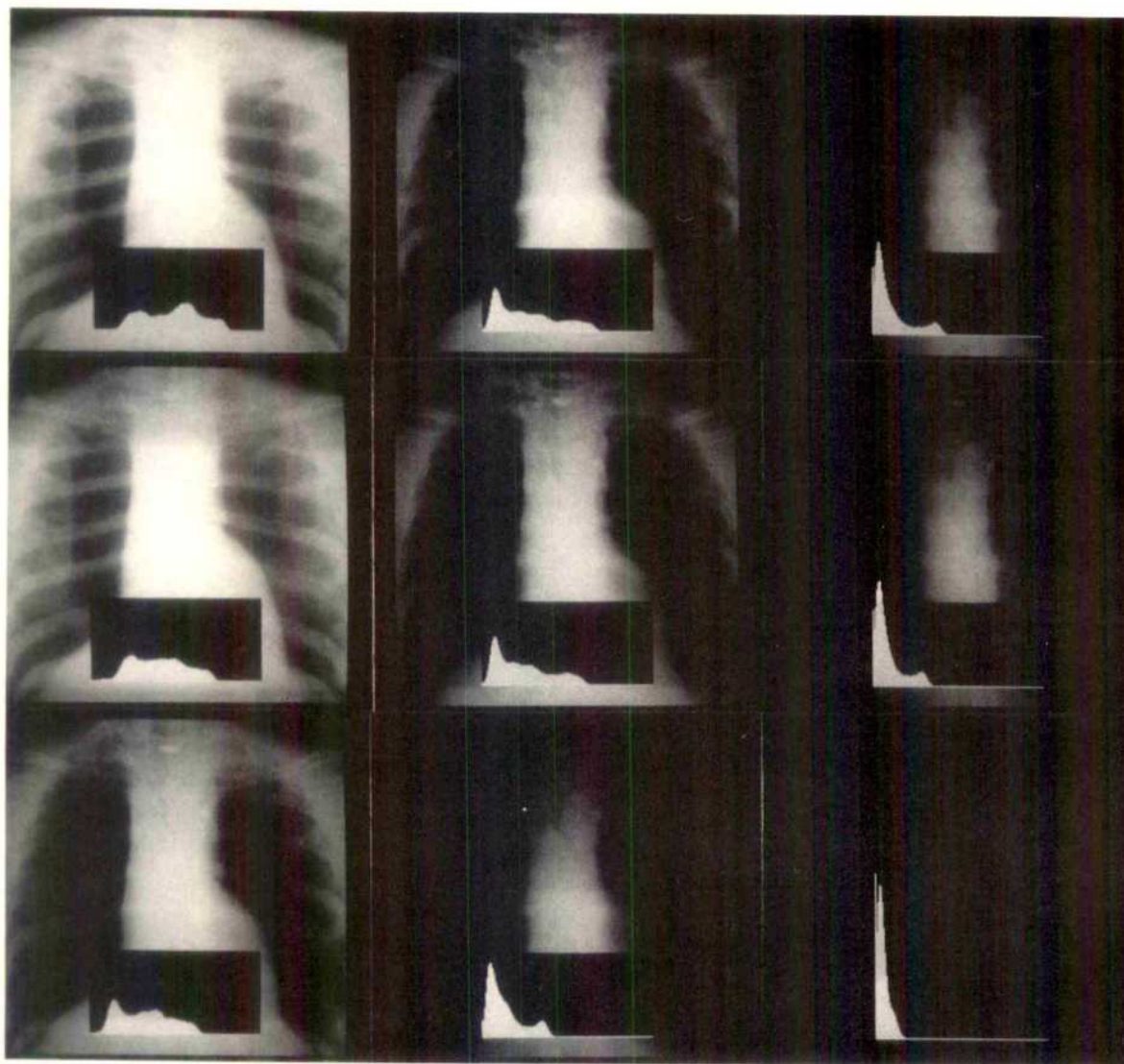


Figure 1. Unprocessed digital radiographs of a chest phantom. Contrast ranges from low to high from top row to bottom row, with kilovoltages of 50, 60 and 75 kV. Exposures are, from left to right, 50, 100 and 200% of optimum. Image histograms are inset.

panel, a monochrome television camera, a signal digitizing unit, an IBM PC-XT microcomputer and an additional, high-resolution graphics display. Each radiograph was placed on the viewing panel and examined by the television camera interfaced, through the digitizing unit, to the computer. The frame grabbing process was fast, requiring only a few seconds, and each image was stored in 512 by 512 pixels, each digitized into a nominal 128 grey scales (Fig. 1). The camera aperture and the conversion gain of the digitizing circuitry were adjusted to produce optimum contrast in the digitized images, and the camera focus was adjusted to provide optimum system resolution, using the software method of Tait (1988). The final optimized

images were displayed on a 512 by 512 pixel array with 256 grey scales, or intensity levels, as shown in Fig. 2, which also includes the image histograms.

The effects of non-uniformity in the illumination panel and in the camera sensitivity were observed by digitizing the image of a uniform transparency with expanded low-level grey scales. These effects were found to be significant but smoothly varying, so they made little impression on the observed local contrast. The system noise was more of a problem, and examination of the analogue signal from the camera indicated that this was the major source. The SNR of the camera was clearly worse than the 40 dB specification published by the manufacturers, so that the effective threshold

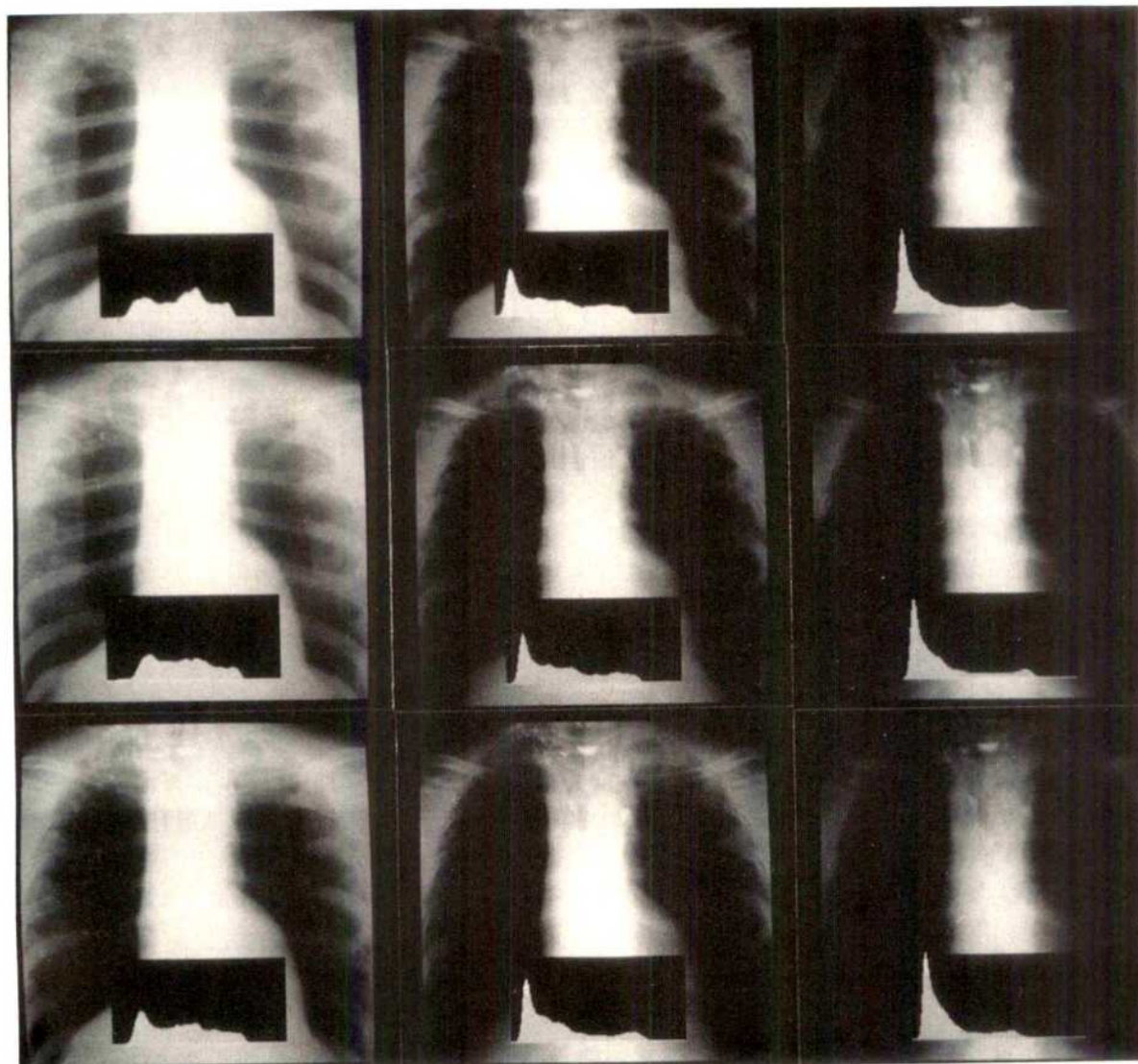


Figure 2. The same radiographs of Fig. 1 digitized with individual software-optimized camera apertures.

contrast measured in a single frame was about 2%. In order to improve image noise, and realize at least 100 grey scales on the display, it was necessary to integrate 32 successive frames to produce a single digitized image, then to subtract a 32-frame background noise level. This agrees with other published conclusions (O'Connor et al, 1984) and indicates that, in general, the camera is a weak link in the film processing system. Replacement of this component by a high-performance unit would be the most direct way to achieve substantial improvement in the performance of the complete system.

A number of contrast enhancement processes were studied and two of these were selected for the project. One was histogram equalization and the other was a process of re-allocating intensity levels to a logarithmic

rather than a linear scale, and is usually described as log registration or log scaling.

These were selected because they were found to have roughly complementary effects on the radiographs used for the investigation. Histogram equalization was found to enhance the visibility of low-intensity display levels, because most of the radiographs showed an asymmetry towards these lower levels before processing. Histogram equalization produces a more uniform distribution, expanding the range covered by these low-exposure pixels. The log scaling process enhanced the visibility of the higher-intensity levels. This, too, is to be expected, since log scaling is equivalent to specifying constant ratios between grey scales instead of constant differences. Since the psychovisual process observes

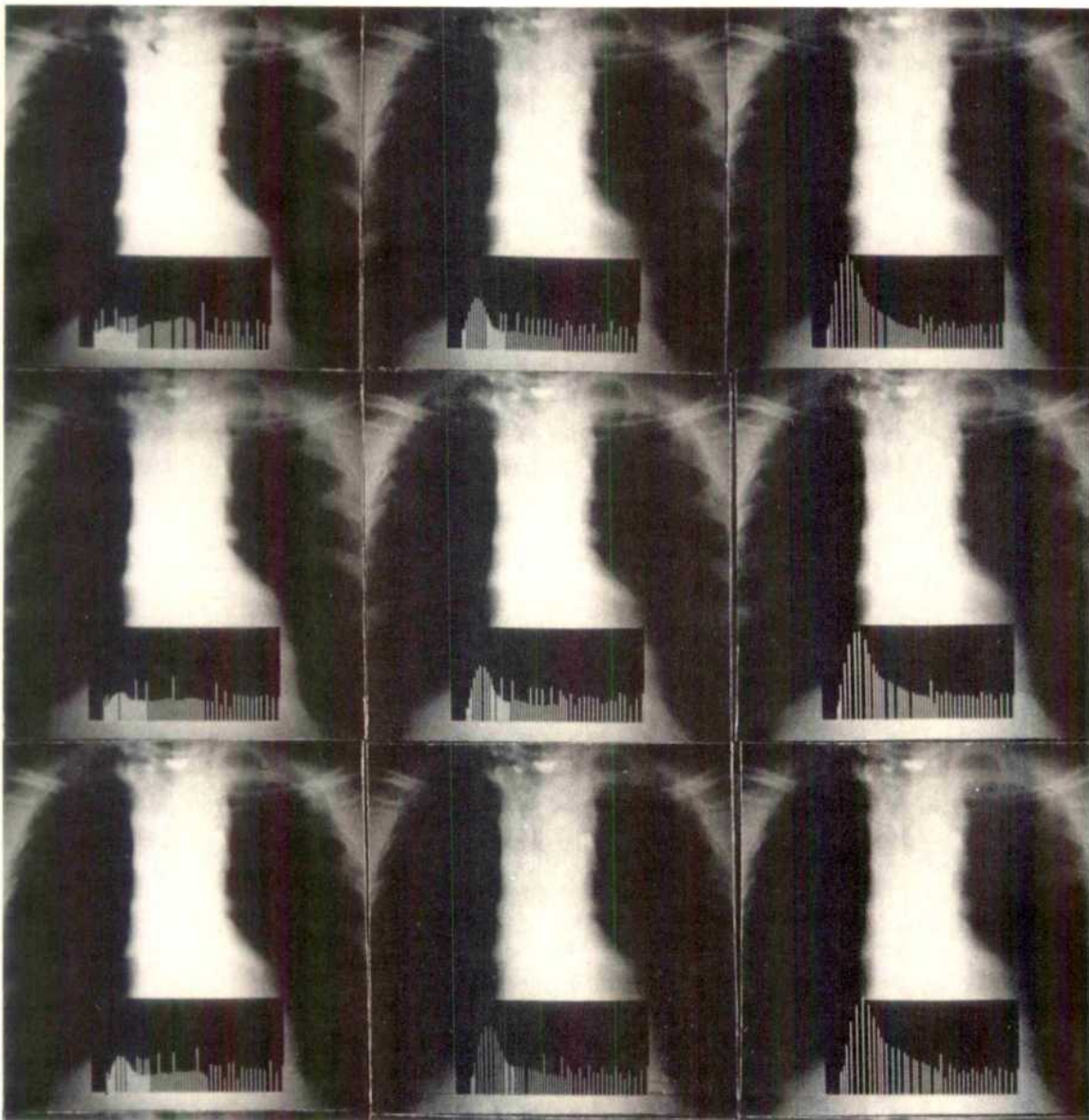


Figure 3. Digital radiographs of a chest phantom processed by histogram equalization and logarithmic scaling. Kilovoltages and exposures are as in Fig. 1.

ratios rather than absolute values, this is advantageous at the high levels, where constant differences would become very small relative differences. The ratio used in the present work provided a constant 1.5% increment between grey-scale levels, which is of the same order as the Weber fraction.

Image assessment

The unprocessed, digitized radiographs are shown in Fig. 1. The optimized versions obtained by separate aperture adjustment are shown in Fig. 2 and those produced by histogram equalization and log scaling are

presented in Fig. 3. The separate effects of log scaling followed by histogram equalization are not illustrated here, but were available for assessment. The systematic effects of these processes are immediately, if subjectively, apparent from the picture arrays, which are shown in the figures.

To test this impression and generate some quantitative measure of image quality improvement, if any, an assessment procedure was designed. A group of observers, consisting of two consultant radiologists, two radiologists, two registrars, three superintendent radiographers and three senior-grade radiographers,

was assembled and shown a series of 36 pictures in a period of about 1 h. These were shown on two monitors driven by the graphics display unit, in random order, and consisted of the nine central elements of the four arrays for unprocessed (but optimized), log scaled and histogram equalized images, along with the double-processed images. The audience was appraised of the nature of the images and asked to view them as attempts at lung-field radiographs. They were instructed to consider each radiograph in terms of the correctness of the overall level of exposure, the overall image contrast and the acceptability of the radiograph in terms of its anticipated diagnostic usefulness. They responded by completing a questionnaire for each image, selecting its category from the following.

- (a) Exposure: heavily under, under, slightly under, correct, slightly over, over, heavily over.
- (b) Contrast: very low, low, slightly low, appropriate, slightly high, high, very high.
- (c) Acceptability: fully acceptable, provisionally acceptable, minimally acceptable, unacceptable.

In order not to perturb any inherent spread of opinion among the members of the panel, no attempt was made to standardize rigorously the meaning of each exposure and contrast category other than to display a few extreme examples as a preliminary exercise. The panel was asked, however, to maintain a consistent individual opinion throughout the viewing session. The term "acceptable" was defined as follows.

1. Fully acceptable. The image should prove suitable, on close inspection, for any anticipated diagnosis.
2. Provisionally acceptable. The image should provide information on most features of interest, but fail on some.
3. Minimally acceptable. Only gross features are demonstrated, and most information is lost.
4. Unacceptable. A repeat exposure is absolutely necessary.

Results

The results of the assessment process are shown in the form of four scattergrams (Fig. 4). The scattergram is defined here as an array of 7 by 7 elements, with each axis calibrated in terms of the seven categories listed above. The vertical axis represents exposure and the horizontal axis depicts contrast. Each individual assessment allocates one count to the appropriate element of the array, whose microstructure is normalized to show these separate allocations. An image collectively assessed as ideal would have all the individual contributions inside the central element, whereas one that evoked general uncertainty would exhibit considerable spread across the array. The overall agreement of the panel is reflected in the deviation of each distribution from its mean, and the location of the mean is a measure of the assessed quality of the process involved. On the chosen scale, the ideal mean would be at values of 3.5 on the exposure and contrast axes.

In this representation, the unprocessed radiographs were found to have a mean exposure assessment of 5.09 and a contrast value of 3.67, *i.e.* a mean estimate of quality that is just off the centre of the scattergram, in the direction of overexposure, as indicated in Fig. 4a. When the images were processed by log scaling, the result was as shown in Fig. 4b, namely, an even more off-centre assessment with exposure and contrast means at 5.36 and 2.49, respectively. The histogram equalized images, represented by Fig. 4c, produced some improvement, however, with means at 4.16 and 4.45, and further slight improvement was obtained with the combination of log scaling and histogram equalization, where the assessments shown in Fig. 4d provide means of 4.46 and 3.94 in exposure and contrast, respectively.

It is also interesting to note that the coefficients of variation of these assessment distributions decrease substantially following histogram equalization or histogram equalization followed by log scaling, indicating a more narrow band of agreement between the observers. The coefficients of variation, that is, the standard deviation divided by the mean value for each group of images, averaged for the exposure and contrast dimensions for the scattergrams described in Fig. 4a-d are 18.5, 18.0, 10.0 and 11.1%, respectively.

An analysis of the acceptability assessments shows some interesting trends. The results have been quantified by assigning a point system to the answers such that 3 points are allocated to "fully" acceptable, 2 points to "provisionally" acceptable, 1 point to "minimally" acceptable and no points to unacceptable radiographs. On this basis, the original, unprocessed images were found to have an acceptability rating of 39.5%. Those subjected to log scaling scored only 19.4%, while the histogram equalized images attracted a mark of 58.1%; the doubly processed images were rated slightly higher, at 63.6% acceptable. The corresponding coefficients of variation for these categories were 63.9, 70.7, 15.2 and 24.8%, respectively. Thus, the doubly processed images scored highest in terms of acceptability, but showed more disagreement, through the coefficient of variation, than the histogram equalized set. The group of images processed only by log scaling was not liked and generated a wide spread of opinion.

Discussion

It is clear from these results that image processing can introduce significant superficial improvement in the subjectively assessed diagnostic quality of radiographs of the type studied in the present work. In itself, this is not an entirely unexpected conclusion, but the fact that the images were digitized, processed and displayed by a microcomputer system is an interesting one. It indicates that, in the opinion of experienced observers, these relatively inexpensive systems can provide measurable diagnostic assistance.

The images used in the assessment procedure were all of the complete chest phantom. It was necessary to limit the range of study in order to compile a substantial number of digitized images, with sufficient variation in

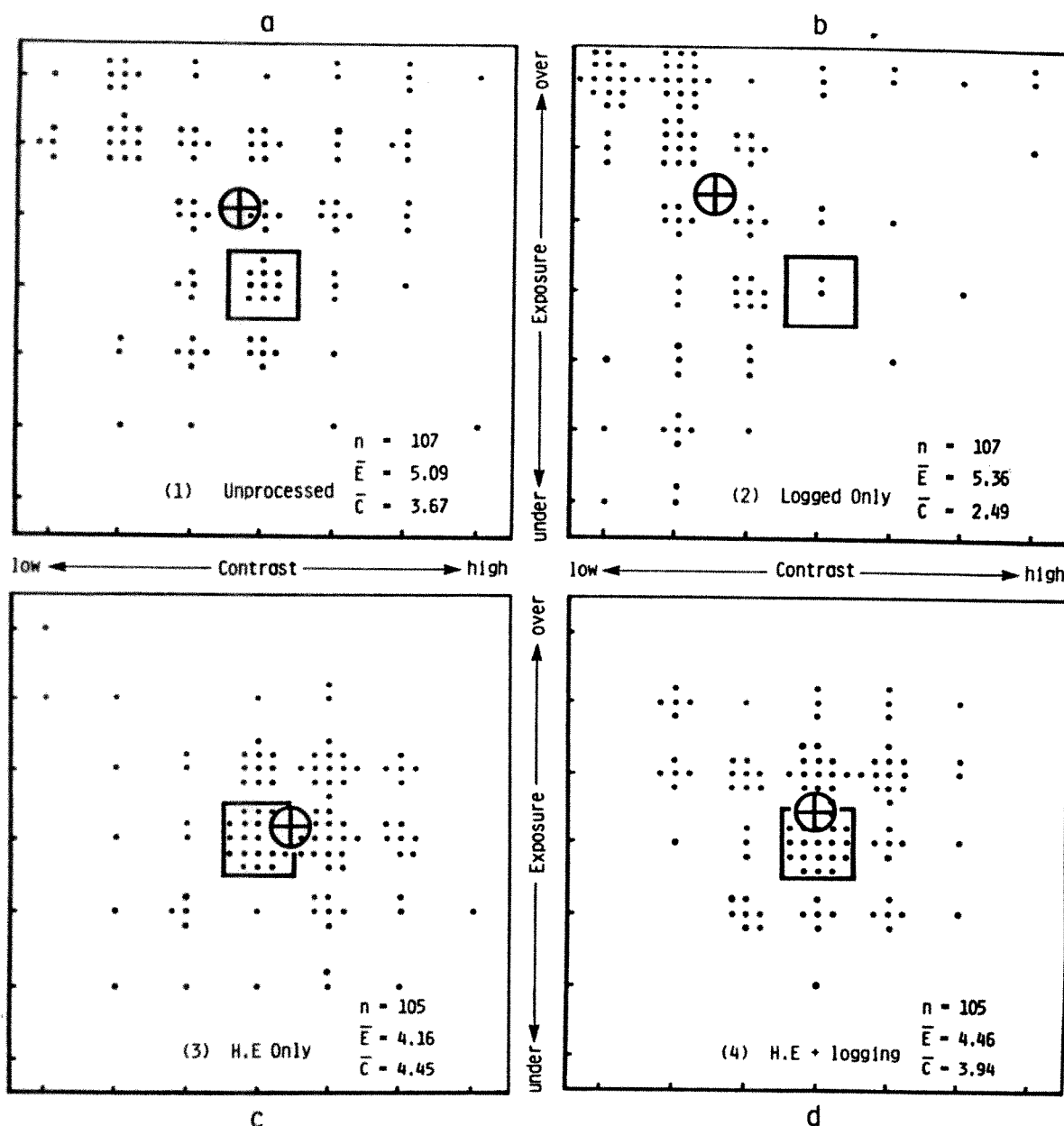


Figure 4. Scattergrams showing the distributions of observer assessment of exposure, varying from underexposed (at the bottom) through ideally exposed (in the middle) to overexposed at the top of each diagram. The contrast assessment varies from left to right as low, through ideal to high contrast.

quality of a single subject to provide statistically reasonable results. The complete radiograph was a convenient stimulus for reaction judgements of the overall effects of the image processes. It is less suitable for demonstrating the full capability of the microcomputer system, since it projects an image of approximately 256 mm cross-section onto a 512 pixel resolution, giving about 2 lines per mm real-scale

resolution. To demonstrate a more realistic 10 lines per mm, small areas of the radiographs can be examined separately.

The method of image assessment was quantitative to the extent of providing a measure of improvement obtained by image processing, but it was not entirely objective. Since the purpose was to explore the viability of microcomputer processing in the clinical

environment, it was a natural decision to rely on the judgement of clinically experienced observers, who were expected to assess the radiographs in terms of their anticipated clinical usefulness. The fact that histogram equalization was strongly favoured in preference to log scaling may be ascribed to the fact that this process was the one that most improved the lower-intensity levels, which are most pertinent to lung-field studies. For this reason, it would be premature to reject the log scaling process as a means of improving radiograph quality. It may be of value for other types of radiograph.

In assessing the effectiveness of the microcomputer system as a means of providing computer-assisted diagnosis in radiography, it is useful to point out the weaknesses of the system. The main one is the television camera whose noise level was a limiting factor in the measurement of grey scales. It is not possible to realize the full 256 levels provided by the digitization circuitry and the display system without an improvement in camera specification well beyond the 40 dB SNR level. An alternative is frame integration. The method of frame integration used in this work would be unduly time-consuming in routine use, but if implemented in hardware rather than software, it could provide an inexpensive solution to the problem of camera noise. Another limitation in the present study was the 512 by 512 spatial resolution of the display. This is the major contribution to total resolution and could be extended closer to 1024 by 1024 with considerable advantage. Several commercially available display systems, suitable for microcomputer configurations, now approach this standard and, used with faster processors than the 4.7 MHz Intel 8088 of the PC-XT, could maintain reasonable processing times.

In conclusion, the results of this preliminary assessment suggest that a microcomputer-based image processing system of the type discussed here may prove a useful and economical addition to a conventional radiographic department as a readily available facility in the viewing area or radiologist's office. Clearly, this suggestion must be pursued by further studies involving, possibly, objective image assessment, subjective response to well defined contrast detail objects, clinical trials, and further equipment development. The latter may involve low-noise cameras or frame integrating hardware, higher-resolution display systems, on-line

image enhancement, and the transmission of radiographic images by telephone.

Acknowledgments

The authors wish to express their appreciation of the co-operation provided by the radiologists and radiographers of the X-ray Department at Charing Cross Hospital, in assessing the diagnostic quality of the radiographs used in the investigation.

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Technical note

A flexible image archiving system using a personal computer and optical disk

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Diagnostic imaging departments generate large amounts of image data from several sources (nuclear medicine, ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), digital radiography). There is often a requirement to preserve the raw data, which creates a need for a stable, large-capacity storage facility. Image archiving facilities are usually provided by the manufacturer of the imaging device and are based on magnetic tape or floppy disks. These are inherently slow and take up a large amount of storage space.

Here, we describe the application of a personal computer and optical disk as an image archiving device, which brings the advantages of large capacity, low cost and savings on storage space.

The problems

Images are stored in a variety of formats, which vary between manufacturers and even between different machines of the same manufacturer.

Image archiving facilities based on magnetic tape have the advantage of large capacity but the data transfer rate is low (approximately 0.1 Mbytes/s), data are written serially so access time is long and the tape reels occupy a large amount of floor space (a busy CT scanner may generate one reel of tape per day). Added to this is the high cost of tapes and the requirement periodically to rewind and rewrite the tapes to preserve image quality.

Floppy disks have significantly faster data transfer rates (approximately 0.5 Mbytes/s) and access time, but will hold only a small number of images per disk, are expensive and they too occupy a large amount of floor space.

Optical disk archiving (Bouwuis et al, 1985), which offers significant savings in media costs and storage space (Kenny, 1979), has been offered as an optional facility on CT scanners for some years (Imasato, 1985) but the drive units are expensive and the widely differing disk standards and formats (Fox, 1986) have delayed their widespread use in imaging departments.

Recently, optical disk systems have become available for use with industry standard microcomputers at very low cost. They offer a compact and flexible alternative to magnetic tapes or floppy disks with very much reduced media costs (Clarkson, 1988) and are suitable for the long-term storage of data (Thomas, 1988).

There is a major problem in interfacing these devices directly to the scanner since any modification to the imaging equipment could invalidate the manufacturer's warranty. Decoding the information stored on magnetic tape or floppy disks provided by the manufacturer can also be difficult because of the variety of formats and data compression algorithms used, and the manufacturers may be reluctant to release details to allow decoding to be achieved.

The solution

An industry standard personal computer with Winchester disk has been adapted to interface with an 8 in floppy disk drive and a 5¼ in optical disk drive. Each drive is supplied with its own interface card, which slots into the computer expansion bus, and with the necessary driver software. The driver software is activated each time the computer is powered up and the drives then appear as extra disk drives to the operating system.

A sector-by-sector copy of the floppy disk to be archived is performed by using the direct sector read facility within the operating system. No decoding of the data held on the disk is necessary.

Although there appear to be a bewildering variety of floppy disk formats, in reality the various combinations of tracks per disk, sectors per track and bytes per sector are limited. In setting the system up for a particular type of disk, each different "legal" combination of these parameters is tried until a successful read is accomplished. The "winning" combination is then stored for future use with these disks. A magnetic tape drive could easily be installed instead of or as well as the floppy disk drive.

The archiving process starts with the recording onto floppy disk of the required data on the scanner. The operator records the file details (patient name, identification number and date) in a menu-driven database, which is held on the hard disk in the microcomputer. A sector-by-sector copy is then made of the floppy disk onto the optical disk. For each record, the database generates a reference pointer through which the data can be located on the optical disk.

To retrieve the data, the patient name and identifier is entered on the database and the file is located on the optical disk and loaded into memory. It is then copied back onto magnetic tape or floppy disk in the same

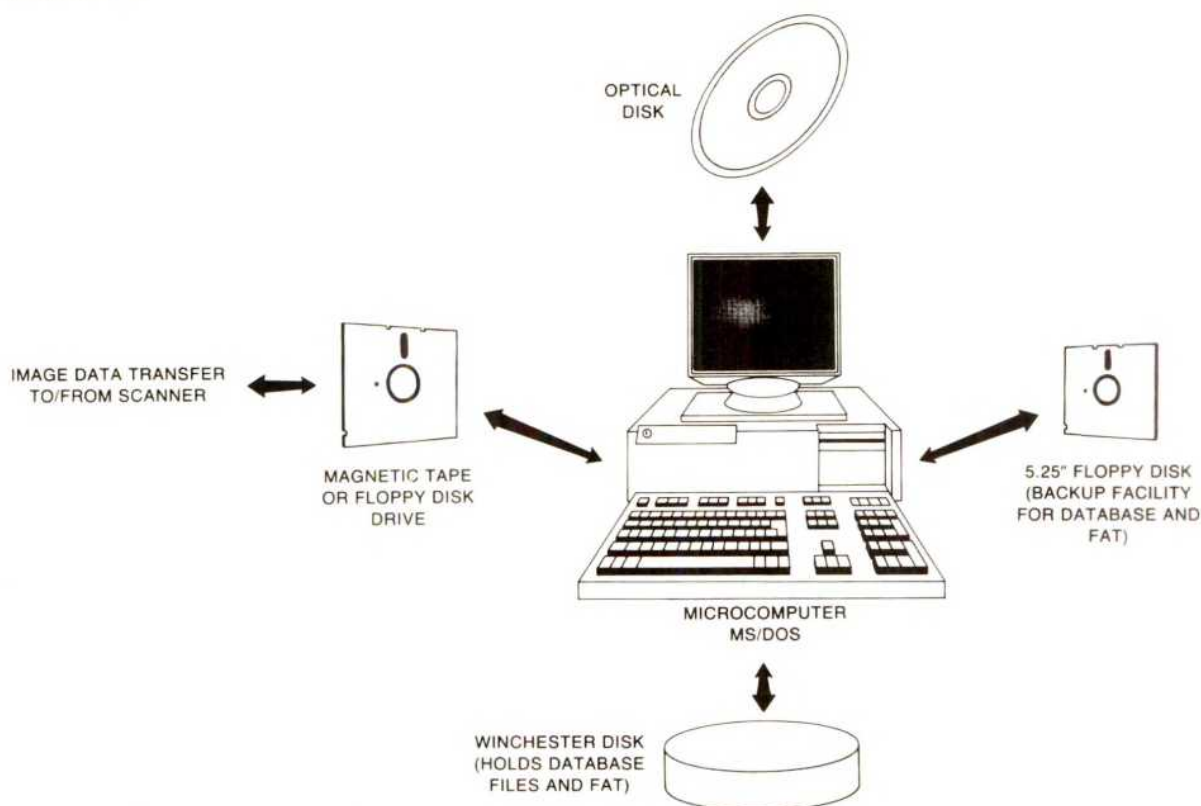


Figure 1. Schematic diagram of the system.

format in which it was read. The images can then be reread into the viewing console of the imaging device. In this way we avoid direct connection of the microcomputer to the imaging device and we can read data from a variety of sources in a variety of formats without needing to decode it.

System specification

The system consists of: (a) an industry standard microcomputer with 1 Mbyte memory, (b) a 40 Mbyte Winchester disk, (c) a 1.2 Mbyte floppy disk drive (5¼ in), (d) an 800 Mbyte optical disk, and (e) software based on the MS/DOS operating system.

In addition, a reel-to-reel magnetic tape drive or 8 in floppy disk drive for transfer of the image data is

interfaced to the microcomputer. The database is menu driven and contains the following information.

1. Patient identifier.
2. Patient name.
3. Date of examination.
4. Optical disk number.
5. Number of floppy disks (some examinations require more than one disk).

The database is resident on the Winchester disk. Each record contains a reference pointer to the optical disk file through a file access table (FAT). A back-up facility for the database and the FAT is provided via the 5¼ in floppy disk. A diagram of the system is shown in Fig. 1.

Table 1. Storage comparisons and cost benefits

Medium type	Storage capacity	Access time	Cost (£)	To store 800 Mbyte	
				No. required	Cost (£)
Optical disk	800 Mbyte	100 ms	100	1	100
8 in floppy disk	512 Kbyte	250 ms	1.25	1600	2000
½ in magtape (800 bpi)	20 Mbyte	> 3 min	15	40	600
½ in magtape (1600 bpi)	40 Mbyte	> 1 min	15	20	300
5¼ in floppy disk	1.2 Mbyte	100 ms	1.00	650	650

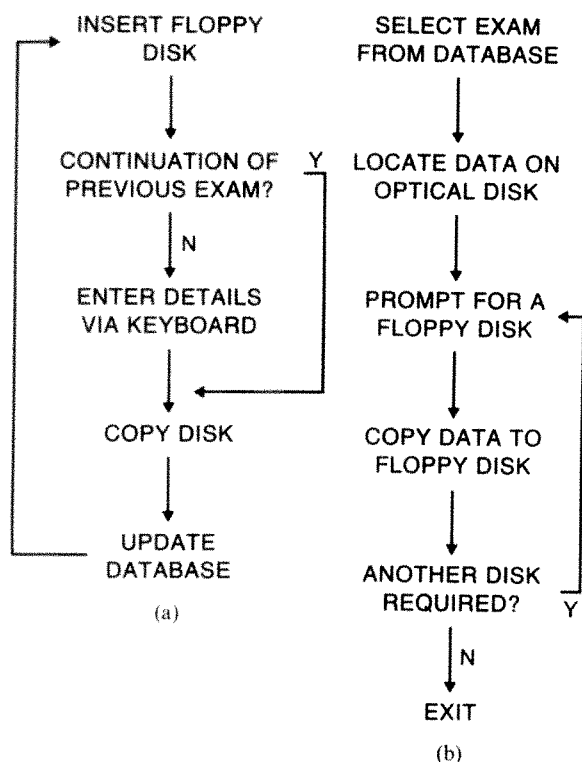


Figure 2. Flow charts of (a) data storage and (b) data retrieval.

System operation

At the end of each working day, that day's floppy disks are read into the PC one by one, using the attached 8 in floppy disk drive. For each disk, the user enters the parameters required to identify uniquely that disk: patient name, patient identifier, date of examination, etc. The microcomputer creates a sector-by-sector copy of the disk onto a blank area of the optical disk. The address of the beginning of the file is generated and recorded on the database with the manually entered details.

The procedure for data retrieval is initiated by the user selecting an examination from the database, either by uniquely identifying the examination, or by selecting

from a displayed range (e.g. from all examinations recorded for a particular patient). The computer then issues a request for a blank floppy disk to be inserted in the drive. The sector-by-sector copy then proceeds, the user being requested for a fresh floppy disk when necessary.

Flow charts for data storage and retrieval are shown in Fig. 2.

System benefits and costs

One 800 Mbyte optical disk in its cartridge occupies less space than a box of 10 floppy disks. Since the optical disk can hold the same information as 1600 floppy disks, the saving on storage space is enormous. There is a concurrent saving in access time; an examination can be recalled in a few seconds from initial request as opposed to a search for the floppy disk number followed by a manual search through many shelves of boxes. Table I indicates the approximate cost of the various storage media available. The relative costs of floppy disk and optical disk storage are approximately 20:1.

Conclusion

This is a very cheap and convenient means of storing large quantities of image data. The capital outlay on hardware is small and the use of industry standard hardware and software ensures the maintenance costs are low. There is no direct connection between the image store and the imaging device and so it can be used with a variety of scanners without decoding the data.

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Case reports

Primary malignant melanoma of the vagina

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(Received December 1988)

Primary malignant melanoma of the vagina is a rare tumour. We report a case, showing the appearances on transverse axial and reformatted sagittal computed tomography (CT), and discuss the management and prognosis.

Case report

A 72-year-old woman who had previously enjoyed good health presented with a 4-month history of passing a little blood per vaginam. She thought she was developing a uterine prolapse, and when the district nurse made an unsuccessful attempt to fit a ring pessary, a lot of vaginal bleeding was noted. Referral to a gynaecologist was arranged. Examination under anaesthesia revealed a large tumour mass involving and occupying the vagina. It did not extend to the pelvic side wall. Physical examination was otherwise unremarkable but a chest radiograph at the time showed pulmonary metastases.

Computed tomography of the abdomen and pelvis was performed with reformatted sagittal and coronal images. A huge tumour was shown in the Pouch of Douglas, involving the vagina and extending into the cervix. The uterine cavity above this was obstructed. No pelvic or para-aortic lymph node involvement was seen but bilateral basal pulmonary metastases were confirmed, liver involvement was noted and the gastric mucosa appeared thickened and nodular. This could also have been due to metastatic involvement.

Histology revealed the mass to be a primary malignant melanoma of the vagina. Palliative radiotherapy with 5 Gy fractions twice weekly to a total dose of 30–35 Gy was commenced.

Two days after radiotherapy was commenced, the patient suffered a cerebrovascular accident and died 2 days later. A post-mortem examination was not carried out.

Discussion

Malignant melanoma is increasing in incidence in the northern latitudes (MacKie, 1983) and causes death of a little over 500 women per year in England and Wales (Registrar General, 1983). The great majority of tumours are of the extremities, and genital tract melanoma accounts for only 3% of the total incidence (Ariel, 1981). Of these genital tract melanomas, only one-tenth are primary melanomas of the vagina, which represent only 2.5% of all vaginal malignancies (Lee et al, 1984).

The great rarity of this tumour has prevented a comparison of treatment methods, but a recent retrospective review of vulvo-vaginal melanoma treated

surgically at the Royal Marsden Hospital (Davidson et al, 1987) has suggested that the prognostic indicators of cutaneous melanoma of the extremities apply to genital tract melanoma. Radical surgery is therefore only appropriate for these patients with a good prognosis as determined by the accurate histological staging of the primary tumour and the presence or absence of satellite nodules and lymph node metastases. Both Breslow (1970) and Clark (1969) have shown the correlation between the depth of invasion of melanoma through the dermis and prognosis. Cutaneous lesions less than 0.75 mm thick have a good prognosis and are probably best dealt with by local excision only, whilst those thicker than 3 mm have a uniformly bad prognosis with distant lymph node and soft-tissue metastases. It may be that patients with lesions of intermediate thickness are those for whom radical surgery is appropriate. However, whilst the overall 5-year survival for cutaneous melanoma is 30–40%, that of vaginal melanoma is only 7% (Lee et al, 1984). This may represent a worse natural history of the disease but more probably reflects the late presentation of

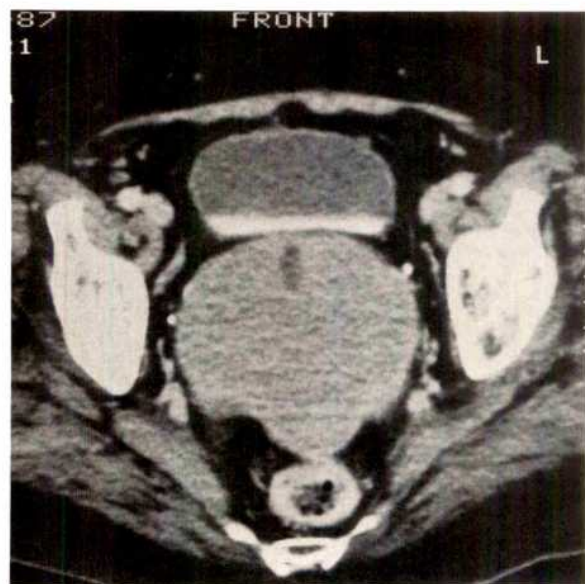


Figure 1. Transverse axial scan showing a large mass of soft-tissue density lying between the bladder and rectum.

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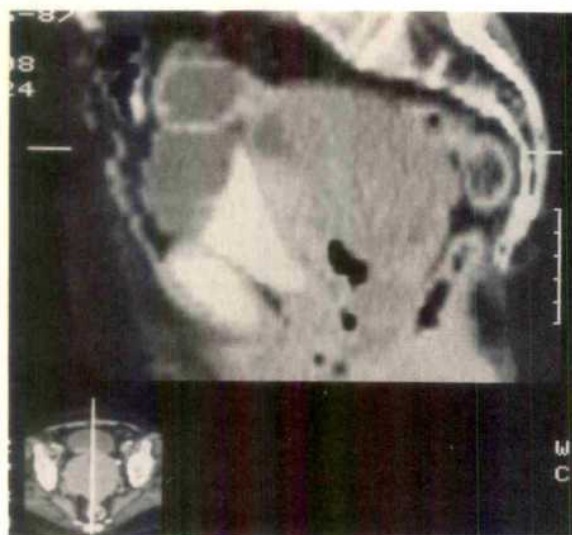


Figure 2. Sagittal reformat at the same level showing in addition the obstructed uterus above the tumour.

melanoma in this site, where attention is only drawn to the disease when ulceration and discharge or bleeding occur.

Neither chemotherapy nor radiotherapy has had much impact on the results of treatment of melanoma at any site although large-fraction X-ray therapy or treatment with fast neutrons may produce an improved

local control rate (Blake et al, 1985; Overgaard, 1985). If those patients likely to benefit from radical surgery can be identified, then the results of treatment may be improved with a lessening of morbidity for those with poor-prognosis disease.

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Neuroblastoma presenting with obstructive jaundice

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Neuroblastoma is the second most common malignant, solid, embryonal abdominal tumour in childhood. In 65% of cases the tumour arises in the adrenal gland, but it can originate from sympathetic tissue anywhere in the body (Kirks et al, 1981). The majority present before the age of 3 years by which time they often have distal metastases to the skull, orbit, bone or liver. We describe a patient with abdominal neuroblastoma, which resulted in obstructive jaundice at the time of presentation. Biliary obstruction occurred secondary to tumour/lymphadenopathy at the porta hepatis causing

compression of the extrahepatic biliary tree. The presence of obstructive jaundice at the time of presentation has not previously been described.

Case report

A 3-year-old boy was referred for investigation of abdominal pain and distension. On examination he was pale and unwell and had a mass in the right hypochondrium. Investigations showed that he was anaemic (Hb 8.8 g/dl). Liver function tests were significantly abnormal with raised bilirubin (30 $\mu\text{mol/l}$; direct, 24 $\mu\text{mol/l}$), elevated liver enzymes and markedly raised alkaline phosphatase (2459 i.u./l). On the day following admission he was noted to be clinically jaundiced.

Ultrasound (Fig. 1) showed a large, ill defined mass containing calcification in the upper abdomen, extending across both sides of the midline and inferiorly down to the

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Figure 1. Supine longitudinal ultrasound scans showing dilatation of the gallbladder and biliary ducts due to a large, ill defined calcified mass in the right upper abdomen. GB=gallbladder; D=bile ducts; K=right kidney; M=calcified mass; F=feet; H=head.

aortic bifurcation. The intrahepatic bile ducts were dilated due to the presence of tumour at the porta hepatis, which resulted in compression of the common duct. The gallbladder was distended. No hepatic metastases were identified. Both kidneys were normal apart from displacement of the left kidney by tumour. Computed tomography (CT) (Fig. 2) confirmed these findings and demonstrated encasement of the coeliac axis by tumour and displacement of the aorta away from the vertebral bodies, features characteristic of neuroblastoma (Faerber et al, 1984). As on ultrasound, the gallbladder and intrahepatic bile

ducts were dilated due to tumour at the porta hepatis; no hepatic metastases were identified but the tumour was considered inoperable.

Needle biopsy of the abdominal mass confirmed the diagnosis of neuroblastoma. Urinary catecholamines were elevated and bone marrow trephine biopsies showed infiltration with neuroblastoma cells. Hence, a diagnosis of Stage 4 neuroblastoma was made. The child was treated with chemotherapy according to the United Kingdom Children's Cancer Study Group current protocol for Stage 4 neuroblastoma. This resulted in reduction in the size of the abdominal mass and gradual disappearance of the obstructive jaundice. The follow-up CT scan confirmed this and showed further calcification in the residual tumour, which surrounded the para-aortic area and major abdominal vessels, therefore, remaining inoperable.

Discussion

Neuroblastoma is one of the most common malignant, solid, abdominal tumours in the paediatric age group, second only to Wilms' tumour (Kirks et al, 1981). In 85% of cases it occurs in the first 4 years of life. The majority originate in the adrenal gland but it may arise anywhere along the sympathetic chain. Tumours arising in the abdomen have a worse prognosis than those arising in the pelvis or thorax (Kinnier Wilson & Draper, 1974). Most neuroblastomas produce excess catecholamine metabolites, which may result in three clinical syndromes: (1) paroxysmal episodes of profuse sweating, flushing, tachycardia and hypertension, (2) diarrhoea and (3) myoclonic encephalopathy (opsoclonus, myoclonus, dancing eyes-dancing feet syndrome) (Merten & Kirks, 1985). Calcification within the tumour occurs in 50% of cases on plain radiographs as compared with 10–20% of cases of Wilms' tumour (Faerber et al, 1984). On CT, 80% of neuroblastomas demonstrate calcification. These round cell tumours metastasize readily and many patients present with metastases to bone, liver, lymph nodes or skull.

The patient we describe had disseminated disease with extensive abdominal lymph node involvement. The characteristic appearances on CT have previously been described (Cremin & Mervis, 1983; Peretz & Lam, 1985). They include, as was the case in the patient described above, the presence of a calcified suprarenal mass extending across the midline to encase the aorta and inferior vena cava. The displacement of the great vessels and encasement is especially characteristic and helps to differentiate neuroblastoma from Wilms' tumour. Although the latter displaces vessels, encasement is not a feature (McDonald & Harwood-Nash, 1971). To date, biliary obstruction in association with neuroblastoma has not been described. However, as neuroblastoma commonly spreads to involve para-aortic and other abdominal lymph nodes, it would seem logical that involvement of lymph nodes in the porta hepatis and peripancreatic regions would result in obstructive jaundice. In practice, intrahepatic metastases occur more frequently than biliary obstruction and this case was unusual in this respect as there were no intrahepatic metastases but there was extensive

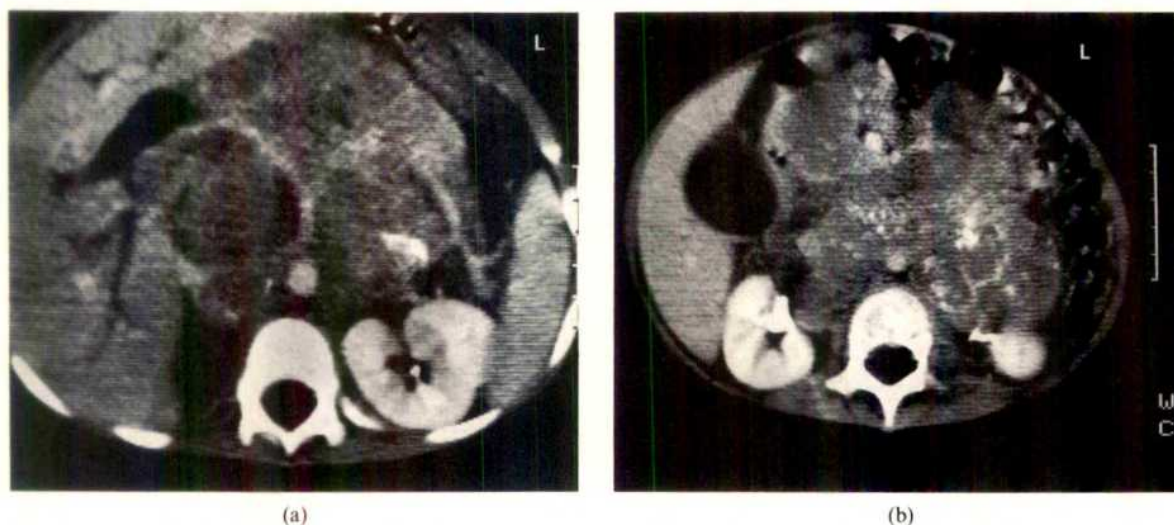


Figure 2. Computed tomographic scans (intravenous contrast enhanced) demonstrating (a) encasement of the coeliac axis by the large calcified tumour and dilated left hepatic bile duct and (b) extent of the mass on both sides of the abdomen and distended gallbladder.

tumour in the upper abdomen, which resulted in biliary obstruction. This unusual occurrence is only likely to be seen in abdominal neuroblastoma and is related to the local mass effect of tumour at the porta hepatis.

Since we described this case we have encountered a similar appearance in a 4-year-old boy with neuroblastoma arising from the coeliac ganglion. Both patients are currently receiving chemotherapy, which often results in good symptomatic relief in cases of advanced disease but cure is only possible in a small minority of these patients. In recent years, there has been an improvement in the 3-year survival rates (Pritchard et al, 1987), but when compared with Wilms' tumour the long-term survival rate remains low.

Acknowledgments

We would like to thank Dr M. Stevens, Consultant Paediatric Oncologist, under whose care this patient was whilst at the Birmingham Children's Hospital.

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Acute aorto-iliac thrombosis in a young man shown on unenhanced computed tomography

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The detection of acute arterial thrombosis on unenhanced computed tomography (CT) at several sites, particularly the intracranial vessels, has been previously documented (Gacs et al, 1983; Vonofakos et al, 1983; Matsumura et al, 1987; Pressman et al, 1987; Hankey et al, 1989). We report a case of acute aorto-iliac thrombosis in a young man in which the typical changes were observed retrospectively in the aorta and left common iliac artery.

Case report

An obese, but otherwise well, 32-year-old man presented following the sudden onset of pain in the lower back that radiated to the left groin and left leg whilst jogging. Clinical examination revealed no positive neurological signs in the lower limbs, apart from subjective alteration of sensation on the outer aspect of the left lower leg and foot. The femoral pulses were difficult to identify at the time of admission but this was attributed to the patient's obesity.

A provisional diagnosis of acute prolapse of a lumbar intervertebral disc was made by the attending clinicians and an urgent myelogram sought. This showed normal appearances.

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Because of the severity of the patient's symptoms, and in the context of the negative myelogram, lower abdominal CT was requested. This examination was performed without intravenous contrast medium and revealed a left iliacus haematoma. In retrospect, the scan also demonstrated increased attenuation within the lumen of the aorta at its bifurcation and within the proximal left common iliac artery, suggesting the presence of arterial thrombosis at these sites (Fig. 1).

Later the same evening, the patient developed visible bruising in the left groin and an urgent aorto-bifemoral angiogram was undertaken. This revealed the presence of a substantial intraluminal filling defect extending distally from the bifurcation to include most of the left common iliac artery as well as an intimal flap in the distal aorta (Fig. 2). The diagnosis of acute aortic dissection with consequent aorto-iliac thrombosis was confirmed at surgery and the patient underwent resection of the affected aorta with insertion of a Dacron graft. Pathological examination of the aortic wall revealed the presence of an underlying granulomatous aortitis. His recovery was uneventful.

Discussion

Increased, intraluminal attenuation on unenhanced CT in the intracranial vasculature as a sign of acute arterial thrombo-embolism is well described. A similar

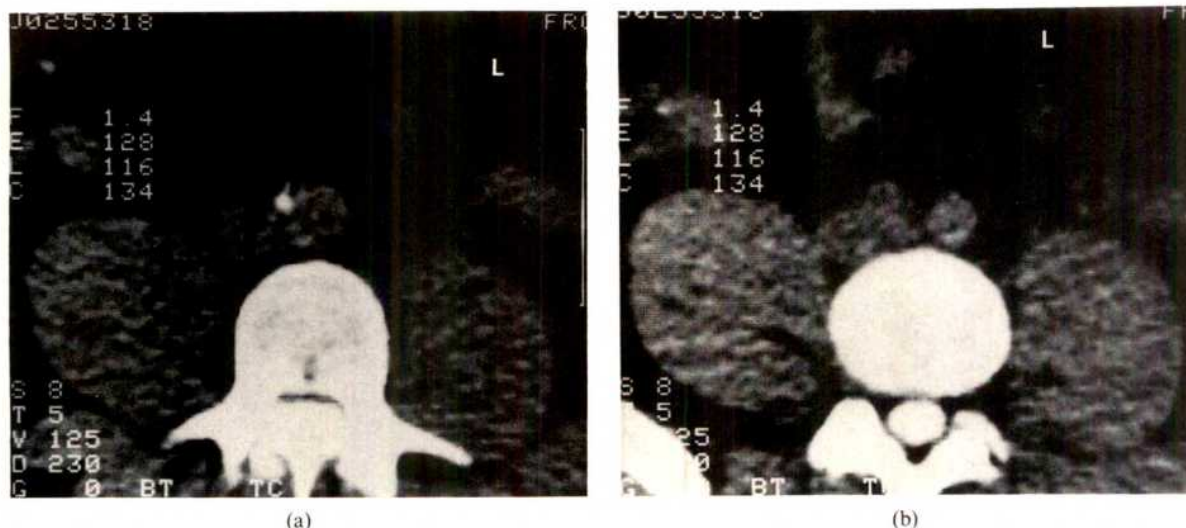


Figure 1. (a) Targeted axial CT scan at L4 without intravenous contrast medium. The abdominal aorta demonstrates increased intraluminal attenuation compared with the inferior vena cava. (b) CT scan 8 mm caudal to (a) showing increased attenuation within the left common iliac artery.

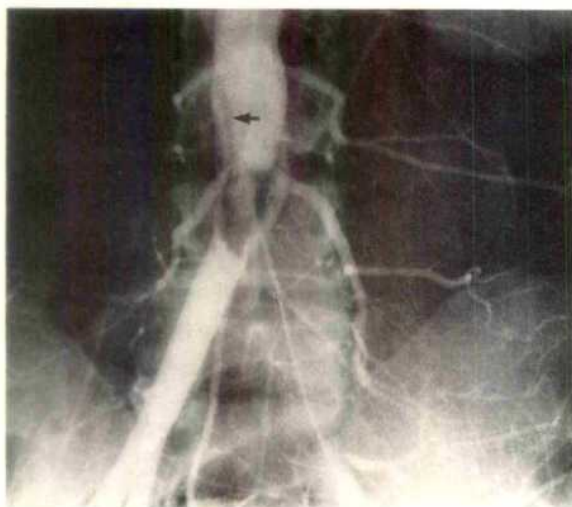


Figure 2. Aorto-bifemoral angiogram showing an intraluminal filling defect commencing at the bifurcation and extending down to involve the entire left common iliac artery. An intimal flap (arrow) confirms dissection as the cause.

finding of focal high density within the arterial lumen was present in our case, subsequently confirmed as representing intraluminal thrombosis.

Acute aorto-thrombosis is a rare event in a young man (Gome, 1953; Kunita, 1978) and thus the diagnosis will tend to be delayed. The serendipitous recognition of the arterial changes on unenhanced CT can potentially hasten diagnosis and treatment in such cases.

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Case of the month

No way out

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A 51-year-old man presented with a 2-week history of painless haematuria following which he had experienced some severe pain in the right groin. Examination was unremarkable. The control radiograph of an intravenous urogram is shown (Fig. 1). Intravenous contrast medium demonstrated diffuse parenchymal loss of the right kidney with partial obstruction of the right ureter. A spot radiograph taken during screening of the lower right ureter is also shown (Fig. 2). Computed tomography (CT) of the pelvis was subsequently performed, which demonstrated the lesion (Fig. 3).

What is the diagnosis? Is there a differential?

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Figure 1. Control abdominal radiograph.

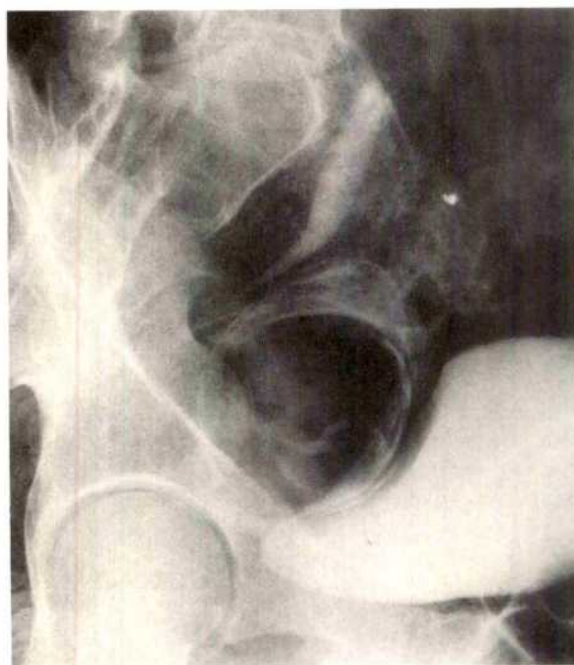


Figure 2. Right anterior view obtained on screening the right hemipelvis.

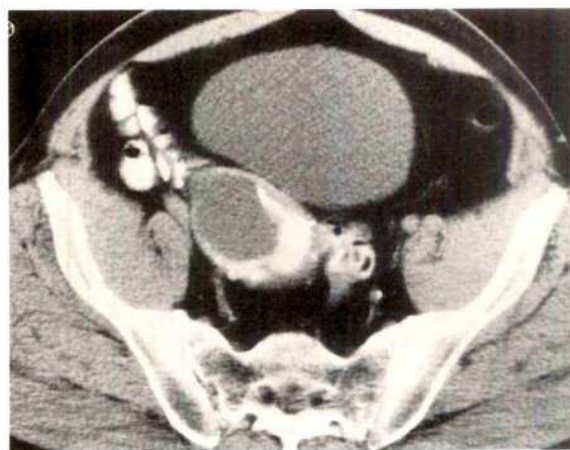


Figure 3. Unenhanced CT scan through the pelvis.

The control radiograph shows a soft-tissue mass with a curvilinear rim of calcification measuring 8 cm in diameter. The oblique view shows that the ureter passes posteriorly to the mass and that the mass itself is separate from, but indenting, an otherwise normal bladder. The CT scan confirms the presence of a cystic mass in the right hemipelvis with calcification in its rim. It appears separate from the bladder and of homogeneous texture with a higher attenuation than urine. It is related to, but distinct from the seminal vesicles and vascular structures. Superiorly, it is apparently contiguous with the caecum.

Laparotomy (undertaken in view of the ureteric obstruction) revealed an adherent appendix mucocoele with an associated polypoid mass in the caecum. This proved to be a carcinoid tumour of the caecum. The appendiceal wall had been replaced by fibrous tissue with patchy bone formation.

Radiographically, the lesion showed several features suggestive of an appendix mucocoele as discussed below. Iliac artery aneurysms may present with curvilinear calcifications in the pelvis, but in this case the mass was shown to lie anterior to the ureter, which renders this possibility unlikely. It may be noted that appendix mucocoele may present as a pulsatile mass (Athey et al, 1984). Chronic abscess or haematoma may develop calcification. Fish and Smulewicz (1981) described an appendiceal abscess with similar appearances on CT, including mural calcification which was causing ureteric obstruction. Similar appearances were seen in another case described by Fish and Smulewicz (1981) but the additional feature of solid components suggested the correct diagnosis of an appendix adenocarcinoma.

In addition, abscesses and tumours are likely to have less well defined margins. Duplication or mesenteric cysts or giant colonic diverticula may present as soft-tissue masses and may have calcification in their walls. In women, uterine fibroids or tubo-ovarian pathology would also be considered.

Discussion

This uncommon finding is rarely diagnosed pre-operatively. Certain radiological findings may suggest the diagnosis (Euphrat, 1947). An appendix mucocoele appears as a well defined, globular, soft-tissue mass, on occasion with calcification in its wall, attached to and displacing the caecum (usually laterally or cephalad). While its location is usually in the right iliac fossa, large masses may present on the left. Non-filling of the appendix on barium enema is usual and, rarely, intussusception of the appendix or mucocoele may be

seen. Its location is usually in the right iliac fossa but large masses may present on the left.

At ultrasonography, the mass appears cystic with posterior acoustic enhancement. An echogenic wall may signify mural calcification. The contents may be anechoic or have a variable echo pattern with gravity dependence and occasionally septations (Athey et al, 1984; Dachman et al, 1985). Internal echoes are presumably due to inspissated mucus.

Findings on CT are those of a cystic mass with or without calcification or septation. Attenuation values usually lie between those of water and soft tissue (Fish & Smulewicz, 1981; Dachman et al, 1985). Computed tomography may also demonstrate the associated condition of pseudomyxoma peritonei.

The exact pathological nature of appendix mucocoeles is debated. The term describes distension of the lumen of the appendix with sterile mucus, which may be associated with obstruction secondary to an inflammatory stricture, carcinoid tumour, carcinoma, appendolith, endometriosis or occasionally extrinsic compression. This, however, is a relatively uncommon situation and more often no obstructing lesion is found. Higa et al (1973) considered that the condition should be regarded as a primary proliferative process: mucinous neoplasms, analogous to epithelial tumours of the colon. He defined three distinct entities, namely, mucosal hyperplasia, associated with only mild dilatation of the lumen, mucinous cystadenoma with some epithelial atypia and marked distension of the lumen, and mucinous cystadenocarcinoma. In their series, mucosal hyperplasia was usually an incidental finding in appendectomy specimens and obstruction of the lumen rare. The latter two categories accounted for the majority of lesions diagnosed as mucocoele and were usually indistinguishable clinically, radiologically and on direct inspection at surgery.

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Short communication

Radiocontrast agents are contact activators of coagulation

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The interactions between iodinated radiological contrast agents and various elements of the blood have been studied by a number of authors (Aspelin & Schmidt-Schonbein, 1978; Almén et al, 1980; Aspelin et al, 1980a, b; Dawson et al, 1983; Dawson, 1985; Dawson et al, 1986; Stormorken et al, 1986; Dawson et al, 1988). Although possible clinical correlates of some of the interactions have been indicated (Almén et al, 1980; Aspelin et al, 1980; Dawson et al, 1983, 1986; Stormorken et al, 1986), most of the work was *in vitro* and performed not so much with practical clinical effects in mind but more with the intention of assessing the absolute and relative chemotoxicities of contrast agents. Haematological effects parallel those of other systems and enzymes and therefore are useful in being relatively easily studied (Dawson, 1985).

Recently, interest in possible clinical sequelae of some aspects of contrast-blood interactions has been renewed (Raininko & Ylinen, 1987; Robertson, 1987). In particular, considerable attention has been focused on the occasional formation of clots in syringes and catheters, which, it has been claimed, is more likely to occur when these contain a non-ionic rather than an ionic agent (Robertson, 1987). This may be explained on the basis that the anticoagulant effects and inhibition of platelet aggregation with collagen of the non-ionic agents are less than those of the ionic agents, consistent with their known lesser chemotoxicity (Dawson & Edgerton, 1983; Dawson, 1985; Howell & Dawson, 1985; Dawson et al, 1986; Stormorken et al, 1986; Dawson et al, 1988). However, it has been suggested that the non-ionic agents might activate coagulation and that this could explain the clots occasionally seen in contaminated syringes. We undertook to investigate this possibility and the results are described below.

Materials and methods

A pool of plasma from 20 normal donors was obtained by collecting blood into 31.3 g/l trisodium citrate in a ratio of 9:1 and centrifuging at 3000 rpm for 10 min. The same pool of platelet-poor plasma was used throughout.

The possible role of radiographic contrast agents in the activation of coagulation *in vitro* was investigated using a modification of the kaolin clotting time. Veronal buffer (pH 7.35) was used as a negative control. The contrast agents sodium meglumine diatrizoate (Urografin 370, Schering AG), sodium meglumine ioxoglate (Hexabrix 320, May & Baker), iohexol (Omnipaque 350, Nycomed) and iopamidol (Niopam 370, E. Merck) were assessed for their ability to initiate the clotting process. The level of activation was measured under four different conditions. Plastic tubes and pipettes were used throughout.

1. One millilitre of neat contrast agent, veronal buffer or kaolin (20 mg/ml) was incubated at 37°C with 1 ml of plasma for 5 min, the mixture being shaken at 1 min

intervals during the incubation period. One millilitre of M/40 calcium chloride was added and after 30 s the fibrinogen was totally removed using bentonite. The absence of fibrinogen in the plasma was verified using Wellcotest latex reagent for fibrinogen degradation products (FDP). It was then frozen at -30°C until the assay was performed. The plasma-buffer mixture acted as a control.

2. Plasma was treated in the same way but with an activation time of 15 min.
- 3, 4. Contrast agents and kaolin were mixed 50/50 with heparinized saline (2 i.u./ml heparin), to mimic the conditions used in clinical practice; the procedures used in (1) and (2) were followed using the diluted contrast medium.

All the treated plasma samples were assayed for fibrinopeptide A (FPA) using an ELISA technique (Boehringer Mannheim), as a measure of the amount of coagulation initiated by the different agents. All assays were performed in duplicate, and on two separate occasions. Very similar results were obtained in all experiments. Results were expressed as ng/ml FPA in the final plasma dilutions.

Results

Table I summarizes the results obtained. It can be seen that FPA is generated in the presence of all contrast agents. Furthermore, at 5 and 15 min and in full strength or 50:50 dilution with heparinized saline, considerably higher levels of FPA are generated in the presence of ionic agents (conventional and low osmolality) than in the presence of non-ionic agents. Indeed, more FPA is generated in the presence of ionic agents at the concentrations used than in the presence of kaolin, the laboratory tool used to activate coagulation in standard tests.

Discussion

These results clearly indicate that iodinated contrast agents are contact activators of coagulation and that ionic agents, both conventional and low osmolality, have a greater effect than the non-ionic agents. This phenomenon has hitherto been unrecognized, but is not unique in that a small number of other substances are known to possess this property (Moskowitz et al, 1970; Morrison & Cochrane, 1974; Fujikawa et al, 1980). The mechanisms underlying it are unclear, but these results show, as in many other studies (Dawson & Edgerton, 1983; Dawson, 1985; Howell & Dawson, 1985; Dawson et al, 1986), that non-ionic agents are closest to the ideal of a totally inert contrast agent.

Activation of the intrinsic pathway through Factor XII is a possible mechanism. The much greater effect of the ionic agents is intriguing in this regard since Factor XII activation may be affected by a number of negatively charged inert surfaces (e.g. glass, silica, kaolin) and a number of negatively charged solutes

Table 1. Fibrinopeptide A levels (ng/ml) assayed in several experiments using different contrast agents, neat and in 50:50 dilution with heparinized saline (2 i.u./ml)

	Veronal buffer	Kaolin	Iopamidol	Iohexol	Ioxaglate	Diatrizoate
5 min activation (neat contrast medium)	2	7	3	4	34	33
5 min activation (50:50 contrast medium/ heparinized saline)	1	8	4	3	17	19
15 min activation (neat contrast medium)	1	15	4	2	44	61
15 min activation (50:50 contrast medium/ heparinized saline)	1	16	2	3	26	22

and colloids (e.g. ellagic acid, dextran sulphate, heparin) (Moskowitz et al, 1970; Morrison & Cochrane, 1974). Direct activation of Factor II or a Factor VII complex-like effect on Factor X are alternative possibilities.

The apparently paradoxical role of heparin in our studies in greatly modifying the results with the ionic agents but not those with kaolin and the non-ionic agents is difficult to explain. Clearly, more experiments are necessary to clarify some of these findings.

These results are likely to make a confused situation worse. It is known that, our new data notwithstanding, contrast agents are anticoagulant in several senses (Dawson et al, 1986; Stormorken et al, 1986) and that non-ionic agents are less anticoagulant than the ionic variety. While the apparently more frequent formation of clots in syringes containing blood-contaminated non-ionic contrast medium (Robertson, 1987) has been explained in terms of their less anticoagulant properties, some angiographers believe that non-ionic agents are, in some unique way, procoagulant. Our work shows that the non-ionic agents do indeed activate the coagulation pathway but to a lesser extent than ionic agents.

The question arises as to whether, in clinical terms, it is better to have a relatively weak contact activator that is also relatively weakly anticoagulant (non-ionic), or to have a relatively powerful contact activator that is also relatively strongly anticoagulant (ionic). The balance of effects may well vary enormously from one situation to another, making the above question unanswerable. We would suggest, as previously (Dawson et al, 1988), that the ideal contrast agent is the inert one and that, broadly speaking, non-ionic agents have significant advantages over ionic agents, but that the true key to safe angiography is good technique.

Conclusions

While contrast agents in many ways are anticoagulant, we have now demonstrated that they are also contact activators of coagulation. Consistent with their greater inertness, non-ionic agents have been found to be much less procoagulant than ionic agents, both conventional and low osmolality.

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(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Are the results of the St Thomas' trial of post-mastectomy radiotherapy inconsistent with the predictions from the linear-quadratic model?

THE EDITOR—SIR,

The St Thomas' experience in post-mastectomy radiotherapy (Bates, 1975; Bates & Peters, 1975) became one of the cornerstones in demonstrating that the nominal standard dose (NSD) formalism (Ellis, 1969), in general, underestimates the deleterious effect of large dose fractions on late-responding normal tissues. It is therefore with interest that we read the 10-year update of the treatment results in this series in the July 1988 issue of *BJR* (Bates, 1988). There are, however, several points where this paper is at variance with the experience from other clinical radiobiological analyses published in the last few years. We would like to discuss briefly some of these.

Dr Bates presents data on five different end-points: late skin changes on the chest wall, subcutaneous fibrosis, impaired shoulder movement, lymphoedema of the arm, and apical pulmonary fibrosis. Two of these, pulmonary fibrosis and late skin changes on the chest wall, appear to have equal average grade of severity in the two fractionation groups. However, some care is advisable in using these two end-points. Establishing dose-response data for pulmonary fibrosis is hampered by the inhomogeneous dose distribution in this region. Different parts of the lung will get different total doses and therefore also a different dose per fraction. The results on late skin changes are also hard to interpret as the scoring of this end-point is a composite factor involving several biological responses in more than one tissue. As a side-remark in this context, the use of average grades for quantitation of late effects should, at least in our opinion, be discouraged as this measure does not separate the effects of incidence and severity. The three remaining expressions of normal tissue injury all seem to be less pronounced in the 6-fraction group and Dr Bates actually points to the apparent advantage of this treatment arm.

Although the following discussion will apply to any of these end-points, we will restrict the discussion to subcutaneous fibrosis, where data from other clinical series are available for comparison. Bentzen et al (1988) found that 4.1 mm was a representative dosimetric reference depth for this end-point, which is quite close to the point of maximum absorbed dose for ^{60}Co at approximately 5 mm. It is therefore quite reasonable to use the maximum absorbed doses and the corresponding doses per fraction in discussing dose-response relationships for this end-point.

From the histograms showing the distribution of severity of subcutaneous fibrosis (Fig. 7, Bates, 1988), the incidence of moderate and severe subcutaneous fibrosis at 10 years is 15.5% and 30.0% in the 6- and 12-fraction arms, respectively. Based on the number of patients at risk in the two arms at 10 years, the difference in incidence can be estimated at 14.5% with approximate 95% confidence limits (0, 30)%. In other words, the hypothesis of equal incidence of moderate and severe fibrosis in the two arms can be rejected ($p=0.05$). The difference at 5 years is even larger: 11% and 41% in the 6- and 12-fraction arms, respectively, i.e. a difference in incidence of 30% with approximate 95% confidence limits (19, 41)% ($p<0.01$).

However, less severe fibrosis in the 6-fraction arm is exactly what is predicted not only by the linear-quadratic (LQ) model

(e.g. Thames et al, 1982) but also by the NSD formula. Assuming an α/β ratio of 2 Gy, Dr Bates calculates that 38.1 Gy delivered in 6 fractions should be isoeffective with 51 Gy in 12 fractions. If the slightly lower α/β estimate from clinical data of 1.8 Gy (Bentzen et al, 1988) is used, the isoeffective dose is estimated at 37.4 Gy. Now the question is whether a 2.4 Gy increase in dose, in a 6 Gy per fraction schedule, may reasonably be expected to yield a 15 to 30% increase in moderate and severe subcutaneous fibrosis. Since no dose-response data are available from the St Thomas' trial, this question cannot be readily answered. Dose-response data from other clinical materials are not directly applicable because of differences in the definition of end-points.

It should be noted that the 51 Gy in 12 fractions arm in the St Thomas' trial would be expected to yield more than 95% moderate and severe fibrosis if the Aarhus dose-response relationship (Bentzen et al, 1988) is used. Similarly, from the Gothenburg dose-response relationships (Turesson & Notter, 1986) an 80-95% incidence of moderate and severe telangiectasia would be expected. This should be compared with a 10-year average score of late skin changes, partly scored on the basis of the occurrence of telangiectasia, at 1.3 on a scale where 1 and 2 correspond to minimal and moderate skin changes, respectively. Thus the St Thomas' scores seem to correspond to relatively more severe radiation sequelae than the scores used by other investigators. In the absence of isoeffect in the two arms of the study, only a lower bound on the α/β ratio can be obtained from this study (Thames & Hendry, 1987). This estimate is α/β greater than -0.8 Gy, which is not a very useful restriction of the range of possible α/β values.

While the isoeffect-dose estimate from the LQ model may or may not be consistent with the observed incidences of subcutaneous fibrosis, the NSD estimate still appears to be an overestimate. Dr Bates calculates from the NSD formula the dose delivered in 6 fractions that should be isoeffective with 51 Gy in 12 fractions to be 41.1 Gy, as opposed to the 35.0 Gy given at St Thomas' Hospital. A 6.1 Gy increase in dose from 35.0 to 41.1 Gy delivered in only 6 fractions would be expected to produce a more drastic increase in incidence of moderate and severe fibrosis than the 15% increase observed in the St Thomas' material. But once again, the lack of isoeffect between the two arms weakens this argument. In contrast, the essential point in the Bates and Peters argument is that the two arms in this study were found to be isoeffective with respect to late complications. A judgement of equal levels of late complications is in itself subject to statistical uncertainty as the hypothesis of no significant difference between the groups may be erroneously accepted because of low statistical test strength, the false negative or Type II error. Nevertheless, the demonstration by Bates and Peters of roughly equal complications in the two arms of the St Thomas' trial was a serious warning to the clinicians about the problems with the NSD formalism.

A much more direct illustration of the inadequacy of the NSD formalism in producing isoeffective doses in different fractionation schemes is provided by clinical studies in which two treatment schedules were set up to have identical NSD but turned out to yield statistically significantly higher proportions of severe late complications in the high dose per fraction group (e.g. Overgaard et al, 1987).

A further point concerns the time evolution of the severity of

late radiation sequelae. Here the findings in the St Thomas' series seem to be partly in disagreement with those of other authors. Late skin changes on the chest wall, evaluated at least in part from the severity of telangiectasia, apparently decrease in severity over time from an average score of 1.8 at 1 year to an average score of 1.3 at 10 years in the 12-fraction arm. This is in contrast to the experience from both the Gothenburg (Turesson & Notter, 1986) and the Aarhus (Bentzen et al, 1989) series, where the proportion of patients with distinct telangiectasia increased significantly with time for 5 to 10 years after treatment. Similarly, the proportion of patients with subcutaneous fibrosis is lower at 10 years than it was at 5 years. Again the experience of others is that subcutaneous fibrosis progresses with time (Spanos et al, 1980; Bentzen et al, 1989) and that these changes are irreversible in the individual patient. One possible explanation for Dr Bates' observations would be that the probability of being alive and getting an examination at 10 years is not independent of the probability of developing late complications.

We conclude that there is no inconsistency between the predictions from the linear-quadratic model and Dr Bates' observations. Although the radiobiological results from this series should be interpreted with care, in view of the methodological problems discussed here, there appears to be a statistically significantly lower incidence of moderate and severe fibrosis in the 6-fraction arm in the St Thomas' trial. This is exactly what is predicted from the linear-quadratic model with an α/β at 2 Gy.

Yours, etc.,
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(Author's reply)

THE EDITOR—SIR,

I welcome the constructive comments of Dr Bentzen and Dr Thames on the St Thomas' dose fractionation trial and agree with them that the linear-quadratic model predicts the less severe late subcutaneous fibrosis found in the 6-fraction arm of the trial. But this is not quite the same as predicting its degree. They suggest that if an α/β value of 1.8 Gy is used, the estimated isoeffect dose for 6 fractions is 37.4 Gy (in contrast to 35 Gy used). Precise data is lacking on the degree of fibrosis following this dose, but clinical experience over more than 20 years suggests that it would be greater than that seen in the 12-fraction arm and may be unacceptable, whereas 35 Gy provided both adequate tumour control and acceptable late morbidity.

Observations of the five normal-tissue end-points were carried out by one observer (T. B.) in the clinic over a period of 16 years (1968–1985). The method of assessing the late skin reactions using average scores failed to show the expected progression with time. This may be due to the fact that the scores were low and very few patients developed marked telangiectasia and/or marked skin scarring (Grade 3), as shown by the photographs. But I believe it is a misinterpretation of the clinical data to conclude that there was less fibrosis in the axilla at 10 years than at 5 years. In the 6-fraction arm, both the

incidence and the degree of fibrosis were slightly greater at 10 years. In the 12-fraction arm, the overall incidence of fibrosis was less but the incidence of severe fibrosis (and also severe limitation of shoulder movement) was greater at 10 years. The average scores at 5 and 10 years were 1.3 and 1.2 for 12 fractions, in contrast to 0.7 and 0.8 with 6 fractions.

From the clinical standpoint, two important messages from the St Thomas' trial should not be lost in the debate. First, in post-mastectomy radiotherapy, large fractions given at the rate of two per week in a short overall time of 18–19 days to a total maximum tissue dose of 35 Gy proved effective and safe. Secondly, the nominal standard dose (NSD) formula must not be used to select the dose when cobalt teletherapy is delivered in two fractions per week. Many radiotherapists wrongly believe that large fractions are *always* associated with less effective tumour control and/or more late normal-tissue damage. Confusion has arisen because doses have been selected on the basis of inappropriate isoeffect formulae or because of attempts to match early reactions and maintain the same overall time. Prediction by the linear-quadratic model is close to clinical observations, but further collaboration is required between radiobiologists and clinicians before it can be used with complete confidence.

Yours, etc.,
THELMA D. BATES

Department of Radiotherapy and Oncology,
St Thomas' Hospital,
London
(Received February 1989)

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Correspondence

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The cost of imaging procedures

THE EDITOR—SIR,

Dr Jeans (1989) asked for reassurance that diagnostic radiology can be financially justified when the possible harm caused by ionizing radiation is costed.

I don't think one needs to involve money in this assessment. For instance, take a large radiation dose examination such as a barium enema. If we take 100 patients aged about 60 years having a barium enema, we would discover about two have cancers. If one of these is then cured we have saved a life. The radiation dose of a barium enema is an effective dose-equivalent of about 8 mSv, giving a population dose of 0.8 Sv for these 100 patients. At a risk rate of 2.5% per Sv—about correct at this age—this will cause 0.02 of a radiogenic death. There is thus a benefit : harm ratio of about 50 : 1, so clearly the barium enema in these patients is justified.

If one starts to use money, an almost unending series of variables is introduced. Some of these are the cost of the examination, the cost of treatment, the cost of alternative methods of diagnosis, the value of a human life, the discounting of the value of harm to be caused in the future, the value of reassurance and of the making of other diagnoses. This all becomes so complicated that the result of such calculations can have little validity.

Valuing the harm radiation causes is important in determining the cost effectiveness of radiation protection. It is also valuable, as in the case which provoked this correspondence, when two methods of diagnosis are available, one using ionizing radiation and one not, and both giving approximately the same diagnostic accuracy.

Yours, etc.,
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(Received February 1989)

Reference

- JEANS, W. D., 1989. The cost of imaging procedures. *British Journal of Radiology*, 62, 194.

Intraoperative localization of an osteoid osteoma

THE EDITOR—SIR,

I was interested in the description of a simple, but apparently very effective, technique to aid in the intraoperative localization of an osteoid osteoma by Todd et al (1989).

I must, however, point out that the radiograph in their paper (Fig. 1) stated to show "no abnormality", quite clearly demonstrates sclerosis of the distal capitulum in keeping with the clinical diagnosis of an osteoid osteoma.

It is disappointing to find such an inconsistency in an otherwise interesting and noteworthy communication.

Yours, etc.,
N. B. THOMAS



Figure 1. Radiograph of the wrist (Fig. 1 of Todd et al (1989)).

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(Received February 1989)

(Authors' reply)

THE EDITOR—SIR,

We thank Dr Thomas for his comments. On reviewing the plain radiograph in question we agree that the distal half of the capitulum is sclerotic. We feel that to say that the appearance "quite clearly demonstrates sclerosis" is perhaps an overstatement. The density of trapezoid is not too dissimilar.

Yours, etc.,
B. TODD

Department of Orthopaedics,
Royal Sussex County Hospital,
Brighton
(Received March 1989)

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Proceedings of The British Medical Ultrasound Society

Twentieth Annual Meeting, held at the Scottish Exhibition and Conference Centre, Glasgow, December 6-8, 1988

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Abdominal ultrasound

Chairmen: W. Hatley and D. A. R. Robertson

- Sonohistopathology of the liver? by A. E. A. Joseph. Abstract not received
- Practical difficulties in duplex scanning of the transplanted liver, by N. Raby, P. Farrant, J. O'Grady, H. B. Meire and R. Williams
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- Duplex ultrasound evaluation of renal transplants: correlation with biopsy, by S. G. MacKechnie, P. Morley, C. D. Sheldon, E. A. McGregor, J. D. Briggs and I. A. More
- Ultrasound findings in renal transplant rejection, by M. L. Nicholson, A. Bell, P. K. Donnelly, P. S. Veitch and P. R. F. Bell
- Practical use of duplex Doppler ultrasound examination of the renal vasculature in critically ill patients in intensive care, by P. E. Stevens, S. J. Gwyther, M. E. Hanson, W. Knox and J. E. Boulton
- Ultrasound assessment of small adrenal masses in bronchial carcinoma, by J. A. Bates and H. C. Irving
- Correlation of indium-111-labelled white blood cell scintigraphy with ultrasonography in detection and assessment of inflammatory bowel disease, by K. T. Khaw, S. H. Savarymuttu, M. G. Cook and A. E. A. Joseph
- Ultrasound as part of a "1 day" gastroenterology service: a pilot study, by E. J. Fitzgerald and P. N. W. Keeling
- The use of disparity in intra- and extrahepatic biliary duct dilatation in the diagnosis of obstructive jaundice, by A. R. Moody, P. Mills, A. Grundy and A. E. A. Joseph
- Diagnosis and presenting symptoms in patients with intrahepatic cholelithiasis, by K. Y. Yip, J. Leung and C. Metreweli
- The achievements and prospects of abdominal ultrasound, by Prof. F. Weill

Practical difficulties in duplex scanning of the transplanted liver

N. Raby, P. Farrant, *J. O'Grady, H. B. Meire and *R. Williams

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Following liver transplantation, clinical and biochemical deterioration may be due to acute rejection or arterial occlusion. Doppler scanning can provide helpful information by demonstrating arterial patency. Doppler ultrasound has been correlated with hepatic angiography in eight cases to determine the accuracy of the ultrasound assessment of arterial patency. Arterial patency was confirmed in all instances. In chronic ischaemia, difficulties may theoretically be

encountered due to the development of a collateral circulation resulting in erroneous interpretation of intrahepatic arterial signals. Since useful information has been obtained from study of the arterial waveform in renal transplantation, we attempted to determine whether the same was true in hepatic transplantation. In a prospective study of 20 patients the intrahepatic arterial and hepatic venous waveform was studied, and six parameters were correlated with the patients' clinical status, liver biopsy results and final outcome to determine whether Doppler assessment can provide any useful clinical or prognostic information. We have been unable to identify any parameter that can reliably distinguish rejection from infection or chronic ischaemia. The possible reasons for this are discussed with suggestions as to how our results may be improved. Assessment to the portal vein is also described. The

site of portal vein sampling is critical and more clinically useful information is obtained from the real-time appearances than the Doppler waveform.

Pitfalls in the interpretation of Doppler studies in the transplant kidney

D. Ll. Cochlin

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Doppler analysis of intrarenal arterial signals is now the gold standard for the detection of acute rejection in the transplanted kidney. Our series of unselected cases show a sensitivity of 92% and a specificity of 96%. This may be improved by considering positive and negative predictive values, which can give virtually 100% values for 90% scans, with less accuracy for studies closer to borderline values. To get this accuracy, however, it is necessary to appreciate various factors that can modify the Doppler signal. Changes in the pulse wave due to central factors — particularly aortic valve disease, bradycardia and aortic aneurysm — modify the signal. Intrarenal arterio-venous fistula following biopsy may give confusing signals and examples of these are presented. The problem of patchy rejection is also addressed. Other workers have published series with lower accuracy, and in particular have suggested that cellular rejection is less accurately detected than vascular rejection. We have not found this in our series. Correlation of Doppler changes with intrarenal pressures show that increased intrarenal pressure is more important than the effect of vasculitis. We believe that the poorer results of other workers are due to bias in interpretation of biopsy data; this is discussed. Finally pitfalls in the diagnosis of transplant renal artery stenosis are discussed. Turbulence near the anastomosis is normal and false impression of high velocity jets can be produced because of acute changes in angle at this level. The value of colour Doppler in this situation is discussed.

Duplex ultrasound evaluation of renal transplants: correlation with biopsy

S. G. MacKechnie, P. Morley, *C. D. Sheldon,

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Duplex ultrasound can be used to detect changes in the arterial blood flow waveform accompanying acute renal transplant rejection, in addition to evaluation of transplant renal artery stenosis. Other forms of renal transplant parenchymal disease are not thought to alter significantly the waveform pattern. Correlative histological data has, however, been lacking, despite the general acceptance of this as the "gold standard" for accurate evaluation. In many cases the clinical course and response to treatment have been used for verification of Doppler results. At our hospital, interval routine biopsy is performed on well functioning renal transplants, in addition to diagnostic biopsy being carried out in all cases of transplant dysfunction. Duplex scans were undertaken within 24 h prior to biopsy in 25 "routine" patients, and in 25 patients with clinical/biochemical evidence of transplant dysfunction, obstruction to urine outflow having been excluded. Waveforms were recorded from the main renal artery at the hilum, and from three separate intrarenal sites. Pulsatility index (PI) was calculated, and a qualitative waveform assessment was also recorded. Results are discussed.

Ultrasound findings in renal transplant rejection

M. L. Nicholson, A. Bell, P. K. Donnelly, P. S. Veitch and P. R. F. Bell

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Despite the recent advances in immunosuppressive therapy, acute rejection remains the central problem in renal transplantation. Clinical assessment of graft size by palpation has always been used as a subjective method of detecting the graft swelling that is a consequence of acute rejection. We have used ultrasound measurement of the cross-sectional area of transplanted kidneys as a more objective assessment of graft size in the diagnosis of acute rejection episodes. One-hundred and forty-one episodes of acute renal allograft dysfunction (creatinine rise of $>30 \mu\text{mol/l}$) were studied in 90 patients. Trucut biopsy under ultrasound control was performed in all cases and 70 episodes of acute cellular rejection were identified. In the absence of a proven urinary tract infection ($n = 7$) or clear pelvicalyceal dilatation ($n = 3$), an increase in graft cross-sectional area of $>10\%$ was defined as a positive scan indicative of an acute rejection episode.

	Biopsy result	
	Rejection	No rejection
Scan result		
+ve	64	7
-ve	6	54

Using this criteria, scanning correctly diagnosed rejection in 64 out of 70 cases (sensitivity 91%) and there were seven false positive scans (specificity 89%). The investigation had a high predictive value when both positive (90%) and negative (90%). This technique is a simple, reproducible, non-invasive test for detecting rejection and deserves more widespread use.

Practical use of duplex Doppler ultrasound examination of the renal vasculature in critically ill patients in intensive care

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*Departments of Medicine, *Radiology, †Radiation Physics and ‡Anaesthesia, Charing Cross Hospital, London*

Critically ill patients who require intensive care are at risk of developing multiple organ failure including acute renal failure. Many of the drugs used to support the cardiovascular system in these patients have potentially deleterious effects on renovascular resistance and renal blood flow. It would therefore be advantageous to have a quick, simple and non-invasive method to assess the effects of vasoactive drugs on the renal vasculature. We have looked at the effect of low-dose dopamine infusion ($2 \mu\text{g/kg/min}$) on the relative blood flow and resistance to flow (as measured by the pulsatility index) in the renal interlobar artery of 12 critically ill patients in the intensive care unit. Duplex Doppler examinations were performed using a Dasonics DRF 400 ultrasound scanner with a 3.5 MHz probe. The kidney was visualized using real-time scanning and an interlobar artery was selected for interrogation. Doppler spectra were recorded before and 1 h after commencing a dopamine infusion. In each case the same artery was interrogated in exactly the same fashion and the angle of the

ultrasound beam was adjusted to maximize the total Doppler signal. All results were paired observations with each patient acting as their own control; the significance of the differences was analysed using the Student's *t*-test. Dopamine infusion resulted in an increase in relative blood flow in every case and this was highly significant ($p < 0.001$). A reduction in pulsatility index was seen in 11 of the 12 patients; this too was highly significant ($p < 0.01$). These results confirm the findings of previous invasive or indirect studies in animals and man. We have shown that duplex Doppler ultrasound can directly study changes in renal blood flow and renovascular resistance non-invasively in man. This enables direct monitoring of the effect of vasoactive drugs on the kidney in the clinical situation and will allow us to manipulate inotropic support to find the regime that gives the best clinical haemodynamic improvement with the least deleterious effect on renal blood flow and renovascular resistance.

Correlation of indium-111-labelled white blood cell scintigraphy with ultrasonography in detection and assessment of inflammatory bowel disease

K. T. Khaw, *S. H. Saverymuttu, †M. G. Cook and A. E. A. Joseph

Departments of Radiology, *Medicine and †Histology, St George's Hospital, London

A study was undertaken to correlate ultrasonography of the bowel with indium-111 white blood cell scintigraphy in order to determine the sensitivity and specificity of ultrasonography in the detection of inflammatory bowel disease (IBD). Eighty scans were performed on 53 patients with histologically proven IBD (12 with ulcerative colitis and 41 with Crohn's disease). The ultrasound assessment was performed within 24 h of the indium scan and the results compared.

The overall sensitivity of ultrasound detection of active sites of IBD compared with the indium scan was 150/178 = 85%. Correlation was highest in the small bowel and lowest in the

Region	False +ve (USS +ve) (Indium -ve)	False -ve (USS -ve) (Indium +ve)	True +ve (USS +ve) (Indium +ve)	Sites detected on USS
Small bowel (excluding terminal ileum)	1	3	22	22/25 (88%)
Terminal ileum	0	1	37	37/38 (97%)
Ascending colon	1	4	29	29/33 (88%)
Transverse colon	3	3	19	19/22 (86%)
Descending colon	2	2	15	15/17 (88%)
Sigmoid colon	1	2	18	18/20 (90%)
Rectum	1	13	10	10/23 (43%)

Ultrasound assessment of small adrenal masses in bronchial carcinoma

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Bronchial carcinoma may metastasize to the adrenal glands, which can be routinely demonstrated during an upper abdominal ultrasound survey. We have prospectively investigated 250 consecutive patients presenting with bronchial carcinoma, using a real-time mechanical sector scanner (Siemens Sonoline SL), and have obtained visualization rates of 99% for the right adrenal gland and 92% for the left. In 16 patients, adrenal masses were large, bilateral and/or accompanied by evidence of metastatic disease in the liver or para-aortic lymph glands. However, in 22 patients, a small (less than 3 cm diameter), solitary adrenal mass was discovered during an otherwise normal ultrasound examination. In these cases the distinction between adrenal metastasis and an incidental benign adrenal adenoma is of crucial importance to patient management, and neither CT scans nor adrenal scintigraphy have been of help in solving this dilemma. We have therefore attempted to assess the significance of these small solitary adrenal nodules by performing serial ultrasound studies and ultrasound-guided biopsies, and by studying the incidence of small solitary adrenal nodules in a control group of 100 consecutive patients referred for upper abdominal ultrasound with other non-malignant conditions.

rectum. If the rectum (which is easily assessed clinically) is excluded, the sensitivity rises to 130/155 = 91%. There were nine false positives on ultrasound, with an overall specificity of 95% (150/159). Two different patterns of wall thickening were recognized. Crohn's disease usually showed a well marked hypoechoic wall (the "Crohn's-type" pattern). Ulcerative colitis was usually associated with less distinct walls where the lumen was not well demarcated (ulcerative colitic or "mucosal-type" pattern). This "mucosal-type" pattern may also be recognized in other inflammatory colitides such as salmonella, cytomegalovirus and pseudomembranous colitis. The results show that ultrasound is an accurate method of assessing disease distribution in inflammatory bowel disease.

Ultrasound as part of a "1 day" gastroenterology service: a pilot study

E. J. Fitzgerald and *P. N. W. Keeling
Departments of Radiology and *Gastroenterology, St James' Hospital and Trinity College, Dublin

Ultrasonography was introduced (as clinically indicated) for a trial period of 6 months for patients referred to a "1 day" gastroenterology clinic. During that period 259 patients had ultrasound examination. The examination was normal in 169 cases (72.6%). In the remaining group, cholelithiasis was the commonest finding (31 cases (12%)). Ten patients had renal cysts varying in size from 1 to 8 cm. In the remainder there was

a wide variety of pathology including malignancy in 14, renal pathology including calculi, hydronephrosis and an angiomyolipoma occurred in nine cases. Sixteen cases had dilated bile ducts; in three of these, calculi were seen within the ducts. Thickened bowel was present in eight cases, a normal pregnancy in one and adrenal masses in two others. The presence of ultrasound as part of the clinic was felt to be extremely important both in confirming the clinical impression of irritable bowel disease and in demonstrating the presence of significant pathology in 27% of cases. This is close to reputed figures (Colquhoun et al, 1988) and indicates that the presence of ultrasound within the clinic does not result in inappropriate referrals. Problems in organizing such a service are described, as are the staffing requirements. These extend well beyond the session originally allotted for this study and therefore those contemplating setting up such a service should include this in their submission for staffing and revenue.

Reference

- COLQUHOUN, I. R., SAYWELL, W. R. & DEWBURY, K. C., 1988. Analysis of referrals for primary diagnostic abdominal ultrasound to a general X-ray department. *British Journal of Radiology*, 61, 297-300.

The use of disparity in intra- and extrahepatic biliary duct dilatation in the diagnosis of obstructive jaundice

A. R. Moody, P. Mills, A. Grundy and A. E. A. Joseph
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Ultrasound scanning is often the first mode of imaging in a patient with jaundice. Identification of obstructive jaundice by the presence of dilated bile ducts is readily appreciated. However, the lesion causing the obstruction cannot always be identified, especially if the lower end of the common bile duct (CBD) is not visualized. In our ultrasound practice we have used the presence or absence of disparity between intra- and extrahepatic duct dilatation as a guide to the obstructing lesion. As predicted by Laplace's law a tubular structure will commence dilatation at the point of maximum diameter when subjected to a rise in intraluminal pressure. Acute obstruction of the biliary system, as with a CBD stone, will result in early dilatation of the CBD, with less marked intrahepatic duct dilatation (i.e. disparity of dilatation). A system under prolonged pressure (as from a carcinoma of the head of pancreas) will exhibit generalized dilatation. In order to test our ultrasound observations, we studied 31 patients with obstructive jaundice, either due to carcinoma of the head of pancreas or CBD stones. Using percutaneous transhepatic cholangiography (PTC) as the "gold standard" the degree of disparity between intra- and extrahepatic bile ducts was assessed for each group. The first order branches of left, right and dorso-caudal branches of the main hepatic ducts were measured and averaged. The common bile duct was measured at its widest point. The ratios of the intra- and extrahepatic duct measurements for the two groups were as follows.

	Mean	Range	SD
CBD stones	4.04	3.45-5.17	0.53
Carcinoma of the pancreas	2.76	1.78-4.22	0.66

A paired *t*-test showed a significance level of $p < 0.001$. The presence of disparity in bile duct size in a patient with obstructive jaundice should therefore suggest an acute onset as caused by CBD stones, whereas lack of disparity is a feature suggestive of longer-standing obstruction, as from carcinoma of the head of pancreas.

Diagnosis and presenting systems in patients with intrahepatic cholelithiasis

K. Y. Yip, J. Leung and C. Metreweli
Sha Tin, Hong Kong

Intrahepatic cholelithiasis is common in South-East Asia and is also found in other tropical areas. The diagnosis of intrahepatic biliary calculi according to the literature is best performed by CT or endoscopic retrograde cholangiography (ERC). However, these studies have either been done on small numbers of patients with gross disease (CT) or designed in a way that discriminated against ultrasound (ERC). As a result of our experience with over 150 patients there is no doubt that ultrasound is the imaging investigation of choice. The finding of a highly reflective cluster of echoes, with acoustic shadowing, aligned along the portal system is diagnostic. The only similar appearances are easily differentiated. The patient may be asymptomatic, have attacks of abdominal pain sometimes accompanied by fever and jaundice, or have liver function tests suspicious of biliary obstruction or malignant disease; rarely, there may be chronic pruritis and mimicking of primary biliary cirrhosis. Awareness of these diagnostic possibilities and appearances is essential in the modern world of rapid travel and migration.

The achievements and prospects of abdominal ultrasound

F. Weill
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Apparently there are no limitations to the applications and developments of diagnostic ultrasound. The procedure is employed in the diagnosis of diseases of practically all organs. Doppler is now widely diffused. Endoscopic ultrasound is routinely carried out, at least for pelvic examinations. Intraoperative ultrasound is available in most operating theatres in large institutions. Interventional ultrasound is achieving remarkable results. The quality of images produced by most machines has dramatically improved, making diagnostic ultrasound still more reliable. Thus, in a series of over 300 follow-up examinations in 46 liver transplantations with duplex Doppler we needed to carry out angiography twice only. Colour Doppler is becoming currently available. Reformatting and ultrasound-computed scanners, at least for small parts such as the breast, are reasonable expectations. But on the other hand we should not forget the limitations of the method, which require in some regions of the body and in many clinical situations a multiprocedural approach. We are still powerless with our transducers when air or bone mask a lesion. And, above all, ultrasound lacks specificity, particularly in the differentiation between benign and malignant lesions, unless guided puncture is employed, but the latter has its own limitations because of difficulties in interpreting cytology. Without tissue characterization, ultrasound of the breast, thyroid, and liver tumours remains an approximate method.

Some developments will probably improve the performances in ultrasound in the near future: further improvements in image quality, sometimes paradoxical (*i.e.* lower frequencies in the disclosure of liver lesions); the advent of ultrasound contrast media (fluor, air bubbles); and tissue characterization by Doppler analysis, which colour Doppler renders easier. Anyway, despite its limitations, ultrasound enables one to diminish the overall number of more expensive and aggressive procedures. Despite the blossoming of ultrasound and

introduction of ultrasound and CT, after a few years of increased expenses, the imaging expenses for abdominal examinations remained stable in our institution from 1974 to 1984. On the other hand, overuse of ultrasound in unskilled hands (*e.g.* the so-called "ultrasonic stethoscope") would have exactly the opposite effect and would be detrimental to the reliability, and therefore to the further development, of this efficacious procedure without which many branches of medicine would be paralysed.

Veterinary ultrasound teach-in

Chairmen: J. S. Boyd and F. J. Barr

Clinical applications of echocardiography in veterinary medicine, by J. Bonagura

Small animal abdominal ultrasound, by F. J. Barr

Cardiac ultrasound: clinical equine applications, by J. Bonagura. Abstract not received

Abdominal ultrasound in large animals, by C. M. Marr

Ultrasonography of the equine limb, by C. M. Marr

Ultrasound examination of the mare's reproductive tract, by W. E. Allen

Ultrasonography of the bovine reproductive tract, by J. S. Boyd

Clinical applications of echocardiography in veterinary medicine

John D. Bonagura

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The clinical application of ultrasound has provided a non-invasive method of cardiac imaging and has facilitated non-invasive diagnosis of congenital and acquired heart diseases. By using standard tomographic image planes, quantitative echocardiography (including M-mode studies) can be done in a repeatable manner. Structural and functional cardiac disorders such as valvular stenosis, bacterial valvular endocarditis, hypertrophic and dilated cardiomyopathy, atrioventricular septal defects, pericardial effusion, and cardiac masses can be recognized with echocardiography. M-mode echocardiograms provide very high sampling rates with accurate timing of cardiac motion and can be recorded simultaneously with physiological signals (ECG, pressure waveforms, Doppler-derived velocity/flow data). The introduction of pulsed and continuous-wave Doppler signals to echocardiography has permitted non-invasive acquisition of haemodynamic data. Pulsed Doppler, particularly when processed by colour-flow imaging, offers qualitative information and exact anatomical localization of normal and abnormal blood flow such as that caused by valvular regurgitation, intracardiac shunting, and turbulent ventricular ejection. By using a modified Bernoulli equation (pressure gradient = $4V^2$), continuous-wave Doppler echocardiography can be used to estimate the pressure drop across an insufficient or stenotic valve, or on either side of an atrioventricular septal defect. Thus, the severity of valvular stenosis, haemodynamic consequence of valvar regurgitation, and the "restrictiveness" of a ventricular septal defect can be assessed. It is likely that the measurement of the Doppler velocity-flow integral and the cross-sectional area of an artery can provide volumetric data that can be useful in the assessment of drug therapy.

Small animal abdominal ultrasound

Frances Barr

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Diagnostic ultrasound is potentially a useful technique in the evaluation of abdominal disease in small animals. The parenchymal organs (liver, spleen and kidneys) are readily accessible to ultrasonographic examination. The techniques employed in making a thorough examination of each of these organs are described. In each case the size and shape of the organ can be evaluated, as well as the internal architecture. The normal ultrasonographic appearance of the liver, spleen and kidneys in dogs and cats is discussed, together with the departures from normality recognized as associated with disease of these organs. Much of the lower urinary tract and reproductive tract in small animals also lends itself to ultrasonographic examination. The techniques for examination of the bladder and uterus in the dog and cat, and the prostate in the dog are described and the conditions under which the ovaries of small animals may be visualized are discussed. The gastrointestinal tract is not easy to examine ultrasonographically as gas and mineral within the tract interfere with passage of the sound beam and impair image quality. However, using an abdominal approach, limited evaluation of the fluid-filled stomach and proximal duodenum is possible. The advent of endoscopic ultrasonography has enabled a far more comprehensive inspection of the gastrointestinal tract, and this technique is briefly described. In addition to providing information about the contour and internal structure of abdominal organs, ultrasound allows accurate placement of needles for fluid or tissue aspiration or biopsy. The technique of ultrasound-guided biopsy together with indications and contraindications are covered.

Abdominal ultrasound in large animals

Celia M. Marr

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Abdominal radiography is limited in its applications in large animals because their size produces practical difficulties in achieving radiographs of diagnostic quality. Ultrasonography of the abdomen has several advantages to offer large animal clinicians: it is a non-invasive technique that allows the visualization of the parenchymal organs of the abdomen, providing a suitable acoustic window can be located; both the overall size and the internal structure of these organs can be assessed and localized lesions within these organs can be identified and their solid or cystic nature established. It should be noted that in the investigation of diffuse infiltration of the abdominal organs, in general, ultrasonography is not specific but it can be useful in providing a means for performing guided biopsy. Ultrasonography is not considered to be useful in the investigation of the majority of gastrointestinal conditions. An ultrasonographic unit equipped with a sector transducer with a low frequency (less than 3.5 MHz) is required to perform abdominal ultrasonography. The normal ultrasonographic appearance of the various organs is consistent across the species. The sites for identification of the liver, spleen and kidneys are discussed and examples of a variety of neoplastic and inflammatory conditions illustrated. Particular emphasis is given to the equine abdomen.

Acknowledgments

The ultrasonographic unit used in the Equine Clinical Centre, Glasgow University Veterinary School was provided by an award from The Home of Rest for Horses.

Ultrasonography of the equine limb

Celia M. Marr

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Ultrasonography is a valuable diagnostic aid, which is becoming increasingly widely accepted as part of the investigative protocol for equine lameness. It is complimentary to radiography and is particularly useful in the imaging of the soft-tissue structures of the limb, the tendons and their sheaths, ligaments and muscles. Lesions can be identified and the progression of healing of injuries can be monitored. However it should be emphasized that ultrasonography is a means of evaluation of morphology and its does not assess the functional integrity of these structures. An ultrasound unit equipped with a short-focus transducer with a frequency of at least 7.5 MHz is required for the examination of most of these structures, but transducers with lower frequencies may be required for the deeper structures. Both sector and linear-array transducers are suitable and the merits and limitations of each are discussed. Various methods are available for storage of hard copies of ultrasonographs and these include video, thermal printers and polaroid and multifomat cameras. The practical aspects of image production, the principles of interpretation and commonly encountered artefacts are described. The normal appearance of various structures of the limb and the ultrasonographic features of various lesions are illustrated.

Acknowledgments

The ultrasonographic unit that is used in Glasgow University Veterinary School for examination of the equine limb was provided by an award from The Home of Rest for Horses.

Ultrasound examination of the mare's reproductive tract

W. E. Allen

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When choosing a scanner, the following points (apart from cost) should be considered:

(1) quality of picture; (2) versatility, *i.e.* can both linear and sector transducers be used and what frequency probes are available?; (3) other applications, *e.g.* pregnancy diagnosis in sheep, dogs, pigs, cardiology in dogs and horses, tendon examination in horses; (4) portability; and (5) after-sales care, *e.g.* will the company lend you a scanner/transducer should yours default for any reason after the warranty expires?

Linear transducers are superior to mechanical sector. If a single transducer is bought, 5 MHz should be chosen; 7.5 MHz will give more detail of early pregnancy (<30 days) and some ovarian structures and 3.5 MHz will give more information on pregnancies > 50 days.

Applications include:

(1) ovaries, (a) size, shape and number of follicles, (b) corpus haemorrhagicum, (c) corpus luteum, (d) luteinized follicles, (e) granulosa cell tumour; (2) non-pregnant uterus, (a) oedema in oestrus, (b) intra-uterine fluid (*c.f.* gut and bladder), (c) cysts (*c.f.* pregnancy); (3) pregnant uterus, (a) size of conceptus (*c.f.* cysts), (b) number of conceptuses, (c) position of conceptus, (d) development of embryo and membranes, (e) fetal heart; and (4) late pregnancy, transabdominal scan (3.5 MHz) for fetal and placental well-being.

Ultrasonography of the bovine reproductive tract

John S. Boyd

Glasgow University Veterinary School, Glasgow

Real-time B-mode ultrasound has been used for a number of years to examine the bovine reproductive tract, but predominantly this work has been with 3.5 and 5 MHz transducers to detect pregnancy in the mid to late term. More recently, 7.5 MHz rectal transducers have become available to the veterinarian and more detailed studies of the bovine reproductive cycle can be carried out. In the session on the bovine reproductive tract, the changes occurring in the ovary prior to ovulation can be imaged in detail and methods of scoring the follicle to predict ovulation time can be demonstrated. The process of ovulation has been recorded ultrasonographically and variations in evacuation of the follicle have been detected. Once the corpus haemorrhagicum has been formed, the maturation of the corpus luteum (CL) can be followed and a system of scoring the CL to determine whether it is a CL of pregnancy can be demonstrated. Uterine morphological changes occurring in cycling cows have been followed ultrasonographically and pregnancy detected as early as 9 days. The arrival of the conceptus can be demonstrated and embryogenesis and the envelopment of the fetal membranes followed in detail during the first 30 days. The technology shows great promise in studying the problems of early embryonic loss and uterine and ovarian pathology. Examples of the morphological changes occurring in both the normal and abnormal reproductive tract are demonstrated using slides and real-time video recordings.

Veterinary ultrasound

Chairmen: J. S. Boyd and F. J. Barr

Ultrasound imaging of the reproductive tract of the bitch, by G. C. W. England and W. E. Allen

The changes occurring in the bovine ovarian follicle prior to and during ovulation, by J. S. Boyd, S. N. Omran and T. R. Ayliffe

Variations in the intensity of oedema in the mares' uterus and its relationship to ovulation, by W. E. Allen

Pulsed- and continuous-wave Doppler echocardiography in normal beagles, by J. M. Ndungu, C. Paterson, D. Northridge, J. S. Boyd and M. Murray

An ultrasound method of estimating liver size in the dog, by F. Barr

Assessment of the use of Doppler waveform analysis to monitor peripheral blood flow in the equine limb, by J. S. Boyd and J. Reid

The use of ultrasonography in the investigation of various ligaments of the equine limb, by C. M. Marr, J. S. Boyd and G. A. Munroe

Ultrasonographic diagnosis of equine superficial digital flexor tendon injury: a review of cases, by C. M. Marr, J. S. Boyd, A. G. Matthews, J. Love, S. Love and G. A. Munroe

The application of real-time ultrasound scanning to commercial sheep, cattle and goat production, by A. J. F. Russel

Ultrasound imaging of the reproductive tract of the bitch

Gary C. W. England and W. Edward Allen

Royal Veterinary College, North Mymms, Hatfield, Hertfordshire

Non-toxic metal spheres were attached to the ovarian busae of several bitches to aid in the ultrasound location of the ovaries. Imaging from the flank position allowed the location of the ovaries in close apposition to the lateral abdominal wall, caudal to the kidney. The right ovary was difficult to image because of its cranial location. During pro-oestrus the relatively hypoechoic ovary developed spherical anechoic follicles, which slowly increased in size. From Day 7 of pro-oestrus onwards, follicles rapidly became larger; thickening of their walls occurred from Day 10 onwards, which corresponded to luteinization prior to ovulation. Follicles subsequently became smaller and irregular in outline but maintained the central anechoic cavity until 25 days after the onset of pro-oestrus. It was not possible to observe ovulation because gradual thickening of follicle walls occurs in the bitch, not rapid follicular collapse (Wildt et al, 1977). When the ovaries were removed at laparotomy they had the same ultrasound architecture as the images recorded *in vivo*. The canine uterus was imaged from the midline position, being located dorsal to the bladder. The uterus of pre-pubertal bitches could not be imaged. During pro-oestrus and oestrus the uterus became increasingly hypoechoic with central regions of hyperechogenicity, similar to that seen in the mare at oestrus. The involuting uterus had a characteristic appearance for several weeks postpartum. Cases of pyometra and cystic endometrial hyperplasia were also identified.

Reference

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The changes occurring in the bovine ovarian follicle prior to and during ovulation

J. S. Boyd, S. N. Omran and T. R. Ayliffe

Glasgow University Veterinary School, Glasgow

The reproductive tracts of 10 multiparous dairy cows were examined ultrasonographically on each day between consecutive oestrus periods using a 7.5 MHz linear transducer;

the ovary was imaged repeatedly to reveal detailed changes in the population of follicles. In each cow the follicle destined to be the ovulatory follicle was identified and followed through to time of ovulation. The follicles were scored for size, echogenicity and turgidity and alterations in the nature of follicular image were recorded. The wall of the follicle immediately prior to ovulation assumed a characteristic thickened appearance and the follicular outline could be seen ultrasonographically to be separating from the surrounding stroma. The process of ovulation was followed on video with the resultant formation of the corpus haemorrhagicum. It is hoped that by categorizing these changes prior to ovulation the optimal time for ova collection could be better assessed.

Variations in the intensity of oedema in the mares' uterus and its relationship to ovulation

W. Edward Allen

The Royal Veterinary College, Hatfield, Hertfordshire

Mares' reproductive tracts were examined daily using real-time ultrasound during 63 oestrus periods. At each examination the size of the largest ovarian follicle was recorded and the degree of uterine oedema was assessed. Oedema was distinguished from free intraluminal fluid and recognized by the mottled appearance that it produces in tissue; it was given a score between 0 (no oedema present) and 3 (very marked oedema). The degree of oedema varied throughout oestrus, and became maximal (usually scored as 2 or 3) some time before ovulation. Three of the oestrus periods (which occurred in the springtime) did not end in ovulation. Of the other 60 periods, none had a score of 3 on the day before ovulation, and eight (13%) had a score of 2 on that day. The score had been below 2 (*i.e.* slight or no oedema) for 1 day (26 periods, 43%), 2 days (14 periods, 23%), 3 days (six periods, 10%), 4 days (three periods, 5%) and 5 to 7 days (one period each day) before ovulation; in four of the oestrus period for which data were available for 4, 5 (two periods) and 8 days the score was never above 1. Uterine oedema was stimulated in an anoestrous and an ovariectomized mare by the administration of exogenous oestradiol. In routine stud management the degree of uterine oedema may be helpful in predicting the time of ovulation.

Pulsed- and continuous-wave Doppler echocardiography in normal beagles

J. M. Ndungu, *C. Paterson, †D. Northridge, *J. S. Boyd and M. Murray

*Departments of Veterinary Medicine, *Veterinary Anatomy and †Human Cardiology (Western Infirmary), University of Glasgow, Glasgow*

A group of female beagle dogs, weighing between 9.2 and 10.6 kg, were used for investigations on the blood flow patterns and velocities across the heart valves, using pulsed-wave (PW) and continuous-wave (CW) Doppler flow methods. Blood flow patterns across the atrioventricular and aortic valves, and through the left ventricular outflow tract, were demonstrated with the dog lying in dorsal recumbency and the transducer placed in a left subcostal position, lateral to the xiphoid cartilage. Blood flow in the ascending aorta was also demonstrated from a suprasternal view by CW, and was similar to that obtained from the subcostal view by both PW and CW. Further investigations were also done using several parasternal views. From the results of these investigations, mean flow velocities across the valves and the left ventricular outflow tract, together with the pressure half-times across the atrioventricular valves, were determined, with significant repeatability. The findings indicate that it would be possible to determine the presence of malfunctions in the heart valves and cardiac haemodynamics in general, and thus improve diagnostic echocardiology.

An ultrasound method of estimating liver size in the dog

Frances Barr

Department of Veterinary Surgery, University of Bristol, Bristol

Liver size may alter in a number of primary and secondary liver diseases. For example, hepatic enlargement may occur in association with neoplasia, venous congestion secondary to right-sided heart failure and fatty infiltration. A decrease in hepatic size may occur as a developmental anomaly and in many cases of cirrhosis. Because of the variation in size and conformation of breeds of dog it is often difficult to assess liver size accurately, either by clinical examination or by radiography. Preliminary investigations have been done to determine a single simple ultrasonographic measurement that may be used as an index to liver size. Such a measurement might be used as one indicator of hepatic disease but could also be used to monitor the progression or resolution of a disease process in response to therapy.

Assessment of the use of Doppler waveform analysis to monitor peripheral blood flow in the equine limb

J. S. Boyd and J. Reid

University of Glasgow Veterinary School, Glasgow

A duplex ultrasound scanner was used to determine the parameters for normal vascular flow through selected vessels in equine fore and hind limbs. Each vessel displayed its characteristic signature and variations of this could be produced by alteration to the temperature of the limb and by use of vasodilatory drugs. The reason for the establishment of these parameters was to seek a method of studying the cause and

possible prevention of post-anaesthetic myositis in the horse. Heavy animals placed in lateral recumbency for prolonged periods can display varying degrees of lameness after anaesthetic recovery. The duplex system was used to initiate the studies to discover the effect of posture, duration of anaesthesia and nature of the operating table-top surface on vascular flow. The recordings were played through a spectral analyser to determine factors for impedance and resistance. Early results indicate occlusive problems occurring in vessels supplying the extremities during protracted anaesthetic recumbency.

Acknowledgments

This study was funded by the Home of Rest for Horses.

The use of ultrasonography in the investigation of various ligaments of the equine limb

Celia M. Marr, J. S. Boyd and *G. A. Munroe

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In conjunction with clinical, radiographic and thermographic examinations and appropriate regional anaesthesia, 12 horses were investigated ultrasonographically to evaluate various ligaments. These were the suspensory ligament (six horses), inferior check ligament (six horses), and distal sesmoidean (two horses). Injury was confirmed in all cases of inferior check ligament injury, in four of the six cases of suspensory injury and in one of distal sesmoidean injury. The normal ultrasonographic appearance of these ligaments on transverse images is of homogeneous echogenic structures that on longitudinal examination are represented by closely aligned linear echoes. The echogenicity of the suspensory ligament is less even than that of the other ligaments. Lesions within the ligaments produced anechoic or hypoechoic areas and variable degrees of enlargement when compared with the corresponding structure of the contralateral limb. In one of the cases of inferior check ligament injury this was so extensive that adhesions between the surrounding soft tissues and the ligament produced an acquired flexure deformity. On ultrasonographic examination, the borders of this area were not clearly defined from those of the adjacent structures. Ultrasonography was a valuable aid to diagnosis in all these cases and it was successfully used to monitor healing in five of the cases.

Acknowledgments

This study was funded by the Home of Rest for Horses as part of the Welfare Project "Ultrasonography of the Equine Limb".

Ultrasonographic diagnosis of equine superficial digital flexor tendon injury: a review of 100 cases

Celia M. Marr, J. S. Boyd, *A. G. Matthews, †J. Love,

‡S. Love and §G. A. Munroe

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Diagnostic ultrasound has become increasingly widely used in equine practice to investigate soft-tissue injuries to the equine limb. Its use has been advocated for the diagnosis of tendon, ligament and muscular conditions and its non-invasive nature is advantageous because numerous repeat examinations can be performed to monitor the healing of such injuries with no harmful effects to the operator or the subject under examination. One hundred horses were selected for ultrasound examination following suspected superficial digital flexor tendon injury and showing various degrees of swelling on the palmar aspect of the limb between the carpal and metacarpophalangeal joints. In 90 of these cases this diagnosis was confirmed ultrasonographically and in the remaining 10 horses the swelling was considered to involve the peritendinous tissues only. Fifty-five of the cases were examined within 4 weeks of the onset of the injury and these cases were re-examined at 3-monthly intervals. The remainder of the cases were examined more than 4 weeks after the initial injury and the repeat examinations were performed less regularly. In the acute stages there were varying degrees of enlargement of the tendon and the echogenicity was reduced when compared with normal structures of the limb. As healing progressed, the lesion became increasingly more echogenic. The ultrasonographic findings were compared with clinical and thermographic findings to assess the merits and limitations of the technique. Ultrasonography was considered to have a sensitivity of 90% and thermography had a sensitivity of 79% in the diagnosis of superficial digital flexor tendon injury. False negatives were encountered with thermography but were not found with ultrasonographic or clinical examination.

Acknowledgments

This study was funded by the Home of Rest for Horses as part of the Welfare Project "Ultrasonography of the Equine Limb".

Paediatric ultrasound

Chairmen: Dr G. M. Hendry and Dr M. A. Ziervogel

Ultrasound diagnosis of congenital hip dislocation and dysplasia: 10 years' experience, by R. Graff and Ch. Tschauner
Measurement of spinal curvature and rotation by ultrasound, by T. A. Whittingham, K. Ions, P. J. Saunders, J. Jago, C. P. Oates and M. Leonard

Neonatal ovarian cysts: aspiration or operation, by R. de Bruyn and P. Ignotus

Another cause of neonatal hydronephrosis: ultrasound assessment of duplex kidneys and ectopic ureteroceles, by C. Dicks-Mirreux, P. Ignotus and R. de Bruyn

On-line intermittent cerebral blood flow velocity and blood pressure measurement in neonates, by A. C. Fenton, M. I. Levene, D. H. Evans, F. S. Schlidwein and C. Cornhill

Ultrasound diagnosis of congenital hip dislocation and dysplasia: 10 years' experience

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Landessonderkrankenhaus, Stolzalpe, Austria

Our experience is now based on approximately 42 000 documented hip sonograms since Graf introduced sonography into examination of newborn and infant hips in 1978. The main advantage of this imaging technique is the visualization of soft tissue and cartilage: thus, we can get an exact picture of the anatomy and function of the hip joint at any time from birth on. If certain technical (5 MHz linear transducer) and methodological standards (training!) are fulfilled, we can answer the questions of whether a given hip's development is

The application of real-time ultrasound scanning to commercial sheep, cattle and goat production

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The use of real-time ultrasound scanning in commercial sheep production has been made possible by the application of knowledge on the nutrition of the pregnant ewe. The accurate determination of fetal numbers allows feed inputs to be related to the number of fetuses carried, thereby providing a means of manipulating birth weights and thus reducing levels of lamb mortality. The extent of use of maternal body reserves can also be controlled with greater precision, thereby reducing the incidence of metabolic disorders and ewe deaths. In the 5 years since the first use of scanning on UK sheep farms, the number of ewes scanned annually has increased to more than 4 million (*i.e.* about 25% of the natural ewe flock) and the benefit to the industry is estimated to be of the order of £15 million per annum. Similar considerations also apply to herds of dairy goats, but the major use of the technique in this species has been in the superovulation and embryo transfer programmes used to multiply the numbers of high value Cashmere and Angora goats. Scanning is used to identify non-pregnant recipients that can be reprogrammed and used again in the same breeding season, and to determine the number of fetuses carried by the "scanned recipients" offered for sale. Real-time scanning is also being increasingly used in herds of both beef and dairy cows. In addition to the early and accurate diagnosis of pregnancy and the identification of fertility problems, the prediction of calving dates in herds using natural service has proved to be a particularly useful aid to nutritional management. Recent advances in the *in vitro* culture of bovine embryos is likely to lead to significant numbers of twin pregnancies; scanning will then become an essential tool in the management of pregnant cows.

appropriate for age or not, if it needs therapy or control, and what is the prognosis; fine differentiation in diagnosis provides fine differentiation in therapy! According to Graf's classification there are four main sonographic hip types.

I	Mature hip	
IIa	Immature hip (< 3 months)	} Centred
IIb	Delayed osseous development (> 3 months)	
III	Cartilage displaced cranially	
IV	Cartilage trapped between femoral head and primary acetabulum	Decentred

Each of these main types has distinct morphological criteria and corresponds to certain values of the angles α ("bony roof angle") and β ("cartilage roof angle"). In Austria and Germany clinical and sonographic screening is now neonatal routine; it is a fact that it is *not* possible to diagnose "dysplastic" hips by clinical means alone. There are clinically innocent hips with a "critical" maturational deficit at birth, which will certainly become decentred if they are not treated immediately. A correctly scanned and documented hip sonogram is a definite, clear and objective basis for diagnosis of congenital hip dislocation. "Treating hips without ultrasound is like treating fractures without X-ray" (Dahlstrom, Friberg).

Measurement of spinal curvature and rotation by ultrasound

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An ultrasound method of assessing the degree of rotation and displacement in the spines of scoliosis patients has been developed over the past 3 years. The primary motivation is the desire to find a method that eliminated the need for repeated exposures to X rays, but it has been found that the new method also provides some information that is difficult to obtain from plain radiographs, in particular the rotation of the vertebrae about the longitudinal axis of the spine. A freely held linear array probe is positioned over each vertebra in turn and angled until the ultrasound image shows the vertebral laminae to be parallel to the face of the probe. Measurement of the depth of the laminae below the probe face is made from the ultrasound image by means of a simplified caliper, whilst remote sensors measure the three-dimensional co-ordinates and orientation of the probe, allowing those of the vertebra itself to be calculated by a microcomputer. Two versions of the system have been built, employing different forms of remote sensing. In one, two small lights mounted on the probe axis are viewed by two ceiling-mounted TV cameras. In the other a commercial magnetometer-based position and orientation measuring device is used. A description of both systems is given, with comparisons of the accuracies and operational features of each. Briefly, the camera system gives slightly better accuracy (1° in angle, 2–3 mm in position), while the magnetometer system gives greater operational convenience. Examples of results from over 170 clinical investigations are presented, comparisons with radiographic measurements made and the potential of the technique as an independent means of scoliosis assessment is discussed.

Neonatal ovarian cysts: aspiration or operation

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Until the advent of routine antenatal ultrasound scanning, uncomplicated neonatal ovarian cysts were rarely reported.

More recently, 19 such cases have been reported. In our unit we have seen eight patients with neonatal ovarian cysts since 1980. Four were diagnosed antenatally, two had congenital adrenal hyperplasia and another two were diagnosed post-natally while being assessed for PUJ obstruction, which had been discovered on routine antenatal scanning. A further two patients were not included in the study as they presented with complication. One presented with an acute abdomen due to a ruptured ovarian cyst, the other had an ovarian cyst obstructing an inguinal hernia. Two patients had bilateral ovarian cysts. There is much discussion as to the choice of treatment for these patients, ranging from oophorectomy or cystectomy to conservative management and follow-up with ultrasound alone. Six of our patients had cystectomy or oophorectomy and two were followed-up by ultrasound. It has been suggested that cysts >5 cm are more likely to undergo torsion. In our experience two patients with cysts <5 cm, 3.8 cm and 3 cm, respectively, had undergone torsion. The most reliable sign of torsion was the presence of a fluid/debris level in the cysts. In all our patients with a debris level, the cysts had undergone torsion. This concurred with the reported cases in the literature. We would suggest that if the cyst contains debris, conservative management is unwise regardless of the size. If the cyst is clear, then conservative management with regular ultrasonography and cyst aspiration should be considered in order to preserve as much ovarian tissue as possible.

Another cause of neonatal hydronephrosis: ultrasound assessment of duplex kidneys and ectopic ureteroceles

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The Hospital for Sick Children, Great Ormond Street, London

The problem of a duplex collecting system associated with an obstructed ectopic ureter and ureterocoele is not uncommon in paediatrics. We have reviewed the ultrasound findings of 20 neonates under 12 months of age with a duplex kidney and ectopic ureterocoele seen at the Hospital for Sick Children between September 1982 and September 1987. Approximately half of these were referred with hydronephrosis of one or both kidneys, detected antenatally on ultrasound. All 20 patients had an ultrasound scan as the initial examination. Hydronephrosis of the upper moiety of the duplex kidney and dilatation of the ureter was present in 12 cases. In three cases both the upper and lower moieties of the duplex kidney were hydronephrotic. A ureterocoele was seen in the bladder in 17 cases. Four patients presented considerable diagnostic difficulty because there was marked hydronephrosis of both kidneys and bilateral hydroureters associated with a ureterocoele. Intravenous urograms were carried out in seven patients, and in four patients a duplex system with a ureterocoele was demonstrated. Micturating cystourethrograms were performed in 10 patients and in seven cases demonstrated the ureterocoele. All patients were treated surgically with an upper pole heminephrectomy of the duplex kidney. Follow-up ultrasound scans revealed that in some cases a residual collapsed ureterocoele is visible for some time after the operation. At our hospital an ultrasound examination is the most accurate and least invasive method of detecting the ectopic ureterocoele and obstructed duplex collecting system and is recommended as the initial diagnostic and subsequent follow-up investigation.

On-line intermittent cerebral blood flow velocity and blood pressure measurement in neonates

A. C. Fenton, M. I. Levene, D. H. Evans, *F. S. Schlindwein and †C. Cornhill†

Departments of Child Health and *Medical Physics, Leicester Royal Infirmary and †Doptek Ltd, Chichester

"Minimal handling" is an oft-quoted, oft-ignored maxim in neonatal intensive care. Current methods of measuring changes in cerebral blood flow velocity (CBFV) in neonates in response to procedures, drugs or changes in ventilation entail repeated handling, which may be detrimental to the infant and may limit interpretation of results. A new system is described in which a small, lightweight probe and cable is attached for a period of hours to the infant's skin to record CBFV from the middle cerebral artery (MCA). The information is displayed continuously at the bedside, enabling the effects of changes in, for example, ventilation on CBFV to be seen as they occur. To date, 20 infants of between 25 and 40 weeks gestation have been studied for periods of up to 7 h, and both normal and induced changes in CBFV recorded. The MCA is insonated with a

specially designed flat Doppler probe (diameter 11 mm, depth 7 mm). The system captures 12 s of full Doppler spectrum from which a maximum frequency envelope is derived. Blood pressure from an intra-arterial line is recorded simultaneously. The frequency envelope is split into individual cardiac cycles and the information used to extract various parameters from each waveform. The average values are written to disk and trended on a computer screen. Activation intervals may be preset from 5 to 60 min. It is hoped that this system will enable us to collect much more information on the normal variability and acute changes taking place within the cerebral circulation of the critically sick newborn, whilst adhering to the principle of "minimal handling".

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Cardiovascular ultrasound

Chairmen: J. Weir and A. B. Houston

Doppler ultrasound in vascular diagnosis: where is it really useful? by C. D. Sheldon

Ultrasound screening for abdominal aortic aneurysm, by C. S. Loh, A. V. O. Wu, B. Eyes and I. M. Stevenson

Screening for abdominal aortic aneurysms in patients with peripheral vascular disease, by D. C. Berridge, C. D. M. Griffith, S. S. Amar, B. R. Hopkinson and G. S. Makin

Duplex Doppler examination of the carotid arteries: the early results and comparison with digital subtraction angiography, by P. McCarthy, Y. Morarji and G. G. Hartnell

Colour Doppler flow mapping: cardiac imaging, spatial velocity analysis and flow quantitation, by I. A. Simpson

Doppler assessment of blood flow: where is it going? by B. A. J. Angelsen. Abstract not received

Outpatient transoesophageal echocardiography, by D. F. Ettles, G. A. Wharton and G. J. Williams

Transoesophageal echocardiography, by M. Pye and A. B. Houston

Echocardiography with Doppler in the assessment of mitral valve prolapse, by C. Clout and D. R. Naik

Applications of colour Doppler imaging in obstetrics and gynaecology, by A. D. Christie

Doppler ultrasound in vascular diagnosis: where is it really useful?

C. D. Sheldon

Gartnavel General Hospital, Glasgow

Advances in Doppler technology, such as the introduction of duplex and colour flow scanners, have extended the potential applications of Doppler ultrasound in vascular diagnosis. However, there are only a few areas where Doppler has been accepted as an accurate and cost-effective alternative to more invasive procedures. This presentation reviews the current position of Doppler diagnosis in the United Kingdom, and highlights those areas where it has been established as a useful technique.

Ultrasound screening for abdominal aortic aneurysm

C. S. Loh, A. V. O. Wu, B. Eyes and I. M. Stevenson

Department of Vascular Surgery, Walton Hospital, Liverpool

One thousand two hundred and ninety-three men aged greater than 55 years were invited to take part in an ultrasound scan screening programme for abdominal aortic aneurysm (AAA); 657 men attended for scanning (50.18%). Their age ranged from 55 to 94 years (mean = 63 years 11 months). The abdominal aorta was not visualized in 19 individuals because of excessive bowel gas and in one because of gross abdominal lymphadenopathy. Maximum abdominal aortic diameter ranged from 11 to 52 mm (mean = 20.1 mm); AAAs (maximum diameter >30 mm) were found in 19 individuals

(2.89%). The prevalence of AAA in this study was 1.32% in the group below 65 years of age and 6.4% in the group above 65 years. A follow-up scan has so far shown progression in the size of the AAA in one individual. One patient has undergone successful surgical resection and grafting and two other patients have since died. Ultrasound scan screening for AAA is practicable but should be directed to population above 65 years of age to improve cost effectiveness. Follow-up scans of small AAA will provide further knowledge regarding the natural history of this condition.

Screening for abdominal aortic aneurysms in patients with peripheral vascular disease

D. C. Berridge, C. D. M. Griffiths, *S. S. Amar,
B. R. Hopkinson and G. S. Makin

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We have studied a consecutive series of 104 new patients presenting with either intermittent claudication or ischaemic rest pain in the lower limbs to determine the incidence of aortic aneurysms in this type of patient. All patients with definite or suspected aneurysms were excluded. Eighty-two patients were male (77%), with a mean overall age of 68 ± 9 years. The majority of patients suffered from claudication (61%), the remainder suffering from rest pain alone (28%) or in association with skin necrosis/gangrene (11%). Four patients were found to have aneurysmal peripheral vessels, one of whom subsequently proved to have an abdominal aortic aneurysm. The mean aortic diameter was 1.84 ± 0.38 cm for men, which was significantly higher ($p < 0.05$, Mann-Whitney U-test) than for women (1.66 ± 0.42 cm). For common iliac arteries the mean diameter was 0.9 ± 0.17 cm, with no significant difference between the sexes. Eight (7.7%) examinations of the iliac vessels were unsatisfactory because of the presence of bowel gas (three on the left, five bilaterally). Eight (7.7%) patients, seven male (8.5%, mean age 74 years) and one female (4.5%, 52 years), were found to have asymptomatic abdominal aortic aneurysms. The diameter of the aneurysms ranged from 2.8 to 6.9 cm. Four patients have undergone elective repair, and one died following deterioration of established renal failure. The other four patients are undergoing regular 3-monthly ultrasound examinations to monitor progress. This method of screening has been shown to have a high acceptance rate of 95% (104/110), with a high incidence of asymptomatic aortic aneurysms. Therefore, patients presenting with symptomatic peripheral vascular disease should be considered for routine ultrasound evaluation of their abdominal aorta.

Duplex Doppler examination of the carotid arteries: the early results and comparison with digital subtraction angiography

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Doppler examination of the carotid arteries has been carried out in Hammersmith Hospital since December 1985. Since then, 230 patients have been examined. Two machines have been used: the Acuson 128 with a 5 MHz probe and the Diasonics 400x with a 10 MHz transducer. The criteria applied to carotid disease diagnosis differ slightly according to the

facilities offered by each machine. The main indications for Doppler studies have been transient ischaemic attacks, asymptomatic carotid bruits, major cerebrovascular events and in the vascular work-up of patients about to undergo coronary bypass grafting. One hundred and sixty patients have had digital subtraction angiography (DSA); 42% (67 patients) have had intra-arterial studies and 58% (93 patients) had intravenous DSA. High levels of specificity (approximately 95%) when comparing DSA and duplex Doppler studies were found, and similarly, high levels of sensitivity (98.5%). The possible sources of error and methods of avoiding them are discussed. The current role of Doppler of the carotids in the investigation of patients with suspected cerebrovascular disease at our hospital is addressed.

Colour Doppler flow mapping: cardiac imaging, spatial velocity analysis and flow quantitation

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Colour Doppler flow mapping now allows a real-time spatial appreciation of flow velocities in relation to surrounding structural detail. Using a technique of autocorrelation, it can solve, for Doppler, velocity information at various loci across a portion of the sector, with flow towards the transducer encoded as increasing intensities of red and flow away as increasing intensities of blue. The velocity-variance colour flow map algorithm also overlays green proportional to the statistical variation or "variance" of velocities around the mean. Variance enhances optical visualization of abnormal flow patterns since it is generally associated with turbulence, but can also be affected by other factors such as high-velocity flow, pulse repetition frequency and sample volume size. The presence of spatial acceleration as demonstrated in an *in vitro* model of serial obstruction and identified by computer-enhanced digital velocity analysis can also produce variance in an otherwise laminar flow stream resulting from a sampling error of colour flow mapping. The power mode flow map algorithm encodes colour based not only on flow velocity but also to a large extent on the amplitude of the Doppler signal. The power mode can enhance visualization of low-velocity flow and in combination with digital computer analysis can potentially provide a more quantitative estimation of the severity of valvular insufficiency than the more conventional velocity-variance algorithms. Application of colour Doppler flow mapping to a wide range of clinical problems can enhance diagnosis and provide new insights into the flow characteristics and haemodynamic basis of many cardiac lesions.

Outpatient transoesophageal echocardiography

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A routine outpatient transoesophageal echocardiography (TOE) service is offered for selected patients attending our unit in whom conventional echo-Doppler studies are technically inadequate or inconclusive. Currently, our indications for TOE include suspected endocarditis and prosthetic valve dysfunction, unexplained embolic episodes and intracardiac masses of uncertain aetiology. Transoesophageal echocardiography is performed under intravenous sedation with midazolam, which produces rapid onset of short-lived sedation and amnesia. Availability of the specific

benzodiazepine antagonist flumazenil minimizes the risk of oversedation. Forty-five such endoscopic studies have been performed with a mean duration of 6 min (range 4–10 min) for each examination. No complications have occurred and all patients tolerated the procedure without complaint. The close proximity of the oesophageal transducer to the heart results in high-quality diagnostic images, which allow precise localization and characterization of intracardiac masses and vegetations. The left atrium and atrial appendage are particularly well visualized and can be inspected for thrombus. Transoesophageal echocardiography provides interference-free Doppler colour flow mapping that detects even minor regurgitant flows. In cases of prosthetic valve dysfunction, valvular and paravalvular regurgitation can be easily distinguished and both the site and extent of the paraprosthetic leak specified. Outpatient TOE with colour flow mapping performed under light intravenous sedation is a safe and valuable addition to current diagnostic ultrasound techniques. In selected patients it provides information that is unobtainable using conventional ultrasound or angiography.

Transoesophageal echocardiography

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Transoesophageal echocardiography has been performed on a series of 24 adults and children with valvular and congenital heart disease. The studies of these with mitral regurgitation have provided images clearer than those from precordial positions and this has proved to be of clinical relevance. In those with aortic disease, little additional information has been obtained. In one boy with coarctation in whom colour and spectral Doppler failed to demonstrate the site of the obstruction, oesophageal studies demonstrated the anatomical narrowing and a clear spectral signal. Transoesophageal echocardiography with spectral and colour Doppler can add significantly to the information available from routine studies. Further work is necessary to ascertain its exact value in clinical management.

Echocardiography with Doppler in the assessment of mitral valve prolapse

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Echocardiographic studies using differing criteria for mitral valve prolapse have produced values for its incidence of up to 21%. We felt that the incidence in our area was much smaller and decided to investigate this. Over a 3-year period, all

patients referred to our department for echocardiography underwent detailed examination of the mitral valve using two-dimensional, M-mode and pulsed Doppler ultrasound. The criteria for diagnosing mitral valve prolapse were those of Morganroth et al (1980). Illustrations of these and the use of pulsed and colour Doppler in the assessment of mitral regurgitation will be shown. The incidence of mitral valve prolapse was less than 3%; it did not change with age. Over 70% of patients had associated mitral regurgitation and its presence rose significantly with increasing age. Our results show that mitral valve prolapse is not a common condition. As the patient ages, more than 75% will have associated mitral regurgitation. We suggest that in view of these findings, regular follow-up of patients with echocardiographic evidence of mitral valve prolapse is indicated.

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Application of colour Doppler imaging in obstetrics and gynaecology

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The relatively new technique of colour Doppler imaging (CDI) should be regarded as an extension of both conventional two-dimensional (2-D) imaging and Doppler blood flow waveform imaging. The fundamental difference between simple pulsed wave Doppler (PWD) and CDI is the size of the area/volume sampled. In PWD a small volume (gate) of flow along a single line of sight is sampled. In CDI an area/volume comprising many gates along many lines of sight is sampled. Thus flow (direction and velocities) at many adjacent sites can be imaged. In the generally accepted convention, flow *towards* the transducer is displayed in a spectrum of reds through towards yellow, the progression being related to velocity. Flow *away* from the transducer is displayed similarly in blues/greens. As Doppler signals are at their maximum when the interrogation angles are low, the imaging of umbilical cord becomes easy at all angles, either by 2-D or CDI and hence optimum angles for recording of PWD are easily obtained. This shortens examination time considerably. The obvious applications in obstetrics are: (a) vessels in the umbilical cord; (b) fetal heart structures; (c) vessels in the fetal head and abdomen; (d) fetal "breathing" studies; (e) placental vessels; and (f) uterine vessels.

Obstetric update

Chairman: J. P. Neilson

Central nervous system abnormality, by M. R. Gowland

Fetal echocardiography, by A. B. Houston

Ante-natal diagnosis of abnormalities of the fetal abdomen, by J. R. MacKenzie

Obstetric update: limb measurement, by L. Grant

Obstetric update: the biophysical profile, by M. J. Whittle

Obstetric update: invasive procedures, by D. H. Gilmore

Obstetric update: Doppler ultrasound in perinatal medicine, by A. D. Cameron

Central nervous system abnormality

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Abnormalities of the central nervous system are the largest group of major congenital abnormalities. They are demonstrated at ultrasound examination by their deviation from the normal anatomical appearances. It is therefore necessary first to describe the normal fetal central nervous system anatomy, in particular how it differs from postnatal anatomy. The abnormalities encountered will be, for the most part, abnormalities in embryological development, either failure of closure of the neural tube or abnormalities of diverticulation or cleavage, and for this reason a brief outline of the embryological development is also included. The incidence of the different types of congenital abnormality is discussed and the following conditions are described: anencephaly; encephalocele; spina bifida including Arnold Chiari malformation; hydrocephalus; holoprosencephaly; hydranencephaly; choroid plexus cyst; and microcephaly. The structural changes present in each condition are demonstrated together with the features useful in differentiating them from similar abnormalities. Where applicable mention is made of any commonly associated finding, for example the association of polycystic kidneys and extra digits with an encephalocele in Meckel Gruber syndrome. Prognostic indicators are also given, for example club feet in neural tube defects.

one to a possible abdominal abnormality are mentioned. Abnormalities are considered under the headings of abdominal wall defects, gastrointestinal lesions and lesions of the renal tract. (a) Abdominal wall defects: examples of exomphalos, with its high incidence of related abnormalities, and of gastroschisis are shown. (b) Gastrointestinal tract lesions: duodenal and jejunal atresia are described, the former often being associated with Trisomy 21, and the difficulty in diagnosing oesophageal atresia antenatally is discussed. Diaphragmatic hernia, meconium ileus and several types of cysts are also mentioned. (c) Renal tract lesions: the prognosis and management of these conditions depends on whether they are bilateral or unilateral and they are considered under these headings. The difficulty in confidently diagnosing renal agenesis is discussed, and the Prune Belly syndrome is mentioned. The types of cystic disease are demonstrated and the problems in differentiating a multicystic kidney from a hydronephrotic kidney indicated. Examples of the various types of urinary tract obstruction are shown, including posterior urethral valves and pelvi-ureteric junction obstruction. The desirability of *in utero* drainage procedures and early delivery are discussed and the findings of a recent review of antenatally diagnosed renal anomalies in the West of Scotland in the last 5 years are presented.

Fetal echocardiography

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From 18 weeks gestation it is possible to obtain echocardiographic views of the heart allowing a clear assessment of the intracardiac and great arteries anatomy. The four-chambers view is the most easy to obtain and should allow most significant lesions to be recognized. Great artery anatomy is less easy to demonstrate in the fetus but can be obtained. Fetal echocardiography now allows congenital heart disease to be recognized early in pregnancy and the questions to be considered in the future relate to the advisability of routinely performing such studies.

Antenatal diagnosis of abnormalities of the fetal abdomen

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The normal ultrasound features of the fetal abdomen are described at varying stages of gestation. Factors alerting

Obstetric update: limb measurement

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The limb buds appear at 36–38 days gestational age, as assessed from the last menstrual period. By 42 days the hands and feet start to develop. Primary ossification centres appear in the long bones at 10 weeks and from 12 weeks accurate assessment of limb length should be possible. The femur measurement is as accurate as the BPD, *i.e.* ± 5 days in assessment of gestational age. In order to obtain accurate measurements of the femur it is important to ensure you have the full length of the bone in view. Soft tissue should be visible beyond both ends of the bone and the bone should not appear to merge with the soft tissue at any point. Measurement is made from the centre of the U shape at both ends of the bone, this representing the metaphysis. It has been shown that measurement of the femur is most accurate when the bone is horizontal and this measurement becomes less accurate as the femur becomes more vertical, such that the error may be as great as 25%. If the femur measurement does not agree with the gestational age assessment by other parameters or if the femur appears unusual in any way, all the long bones should be assessed. Anomalies of the limbs are uncommon; local malformations occur with frequency of 1 in 500. Skeletal dysplasias characterized by generalized defective development of bone and cartilage have a frequency of 1 in

5000. However, it is important to measure the femur as part of the routine assessment of every fetus. This helps confirm the accuracy of other measurement parameters and necessitates fuller inspection of the fetus whereby unrelated defects may be noted.

Obstetric update: the biophysical profile

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The biophysical profile was first developed by Platt and Manning as a method of quantifying the fetal condition in terms of activity, breathing movements, tone, amniotic fluid volume and cardiotocography. A score of either 0 or 2 was ascribed to each of these variables as a maximum score would be 10 and a minimum score 0. During the development of this test it became obvious that one of the most useful predictive variables was the depth of amniotic fluid present although in the initial descriptions only pools of less than 1 cm were said to be significant — this has been modified. In general this method of assessment has been applied to the post-dates pregnancies but other high risk cases have also been investigated. The results from large studies, such as those described by Manning et al (1987), indicate that the profile may offer a fairly precise impression of the fetal condition, a maximum score being associated with a perinatal mortality rate within a week of the test of < 1/1000 whilst with a low score the rate could be as high as 600/1000. Since the original description of the technique a number of modifications have been made and although the profile has an important role in fetal evaluation, the clinical circumstances for which it is most appropriate remain unclear.

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Obstetric update: invasive procedures

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The techniques for all invasive procedures (amniocentesis, chorionic villous sampling, fetal blood sampling or drainage of a fluid-filled space) are similar. They therefore share certain manipulative features and it is much more important that the operator be confident with his own "basic" method than that he attempt to mimic others' descriptions of individual procedures. Currently, amniocentesis is the most commonly employed invasive procedure and it will therefore be the one on which the operator fashions his technique for all others. Amniocentesis should be performed under direct, real-time ultrasound control and it should therefore only be performed by someone who has experience of obstetric ultrasonography. After performing routine ultrasound examination for fetal anomaly, an entry path for the needle is selected. If transplacental amniocentesis is necessary, then the deepest pool of amniotic fluid should be used irrespective of the placental thickness traversed. The operator dons sterile gloves, swabs the patient's abdomen with a suitable antiseptic and applies sterile, pre-packed ultrasound jelly. The ultrasound transducer is then placed in its own sterile glove or plastic bag and the path for needle entry is

re-established. Controlling the transducer with the left hand, a 22-gauge needle with stylette is inserted into the liquor pool in one quick motion using the right hand. Local anaesthesia is not necessary. Once the needle is in place, the stylette is removed and 15–20 ml of fluid are withdrawn. The syringe is removed from the needle, which is then quickly withdrawn. The appropriate timing for amniocentesis should be established with the laboratory processing the specimen. Anti-D immunoglobulin should be administered to Rhesus-negative women. For chorionic villous sampling, an entry path that will take the needle through the placental tissue *parallel* to the gestation sac should be chosen. The author uses a single-needle technique. A 20-gauge needle with stylette is passed quickly through the maternal abdomen into the myometrium and alignment checked. It is then passed quickly into the placental substance and the stylette removed. Ten millilitres of intermittent suction is applied using a 20 ml syringe and the needle gently moved up and down to avulse chorionic villi. The needle is then removed, maintaining a small amount of negative pressure, and the tissue obtained flushed into a dish for examination. The procedure can be repeated a second time if need be. If no tissue is obtained after two entries of the needle, then the procedure should be postponed for a further week when it can be repeated. The needle used for fetal blood sampling is also 20-gauge with stylette. A needle path that will enter the cord perpendicularly at its placental insertion should be selected. If this site is posterior or if fetal blood transfusion is to be performed, then fetal and/or maternal sedation may be used to minimize the risk of needle dislodgement during the procedure. The drainage of a fetal bladder, renal pelvis or intra-abdominal or intrathoracic cyst is performed in exactly the same manner, again using a 20-gauge needle with stylette. It is essential that no matter which procedure the operator chooses to perform, he gains experience in pre-termination cases in the first instance. He should also be aware not only of national risk figures for the procedures but also of his own level of expertise and individual risks. Only with such information can prospective patients be counselled adequately, allowing them to make informed decisions.

Obstetric update: Doppler ultrasound in perinatal medicine

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Doppler ultrasound is rapidly becoming an important tool in perinatal medicine. Until recently, inaccessibility of the fetus has prevented examination of the fetal and placental circulations. Most of the present knowledge concerning fetal circulatory physiology has been gained from observations on animal fetuses using invasive and non-repeatable methods. Doppler ultrasound, however, allows a non-invasive and repeatable assessment of both fetal and utero-placental circulation to be performed. The Doppler effect and its application in the study of blood flow are described. A description of pulsed Doppler ultrasound and continuous-wave Doppler ultrasound and the advantages and disadvantages of both systems are stated. The methods used to calculate the various blood flow indices such as SD ratios, pulsatility index and resistance index are described and the problems of quantitative assessment of fetal blood flow addressed. Various factors are known to affect fetal and utero-placental blood flow. A cross-sectional study of 120 patients is presented

concerning the influence of gestational age on human fetal and utero-placental blood flow in the fetal aorta, umbilical artery, inferior vena cava and the arcuate artery in the placental bed. This study in human pregnancy is compared with the influence of gestational age and heart rate in ovine pregnancy. A chronic sheep preparation using atrial pacing to induce fetal tachycardia and hydrops and study the effects on the lamb fetal aortic flow velocity waveform is discussed. Pulsed Doppler ultrasound has a role to play in the management of human fetal dysrhythmias and examples of these are presented. A study is presented concerning the use of pulsed Doppler ultrasound in

41 patients with pregnancy-induced hypertension and intrauterine growth retardation. The results of this study suggest that Doppler ultrasound may prove beneficial as an adjunct to fetal monitoring in high-risk pregnancies. Doppler abnormalities appear to be a more sensitive indicator of fetal distress than the gold standards of fetal monitoring, cardiotocography and biophysical profile assessment. The place of Doppler ultrasound as a screening tool in obstetrics and the possibilities of using colour Doppler flow mapping as another method of fetal monitoring in high-risk pregnancies are addressed.

Physics, instrumentation and bioeffects

Chairmen: J. A. Evans and A. J. Hall

Colour flow imaging, by B. A. J. Angelsen. Abstract not received

The enhancement of cavitation effects by acoustic pulsing and by a relative rotation of the sample and the beam, by T. G. Leighton

The search for free-radical production in the ultrasonic beam produced by duplex ultrasound systems, by D. C. Crawford, A. J. Walton, A. Mortimer, M. Dyson and L. D. Allan

Wound healing acceleration by ultrasound, by A. R. Hosseinpour, R. Hickman, S. R. Young and M. Dyson

Absence of sonoluminescence in the human cheek, by M. J. W. Pickworth, T. G. Leighton, J. Tudor and P. P. Dendy

The potential of seismic migration for medical ultrasound image enhancement, by W. A. Sandham and J. L. Bowie

Determining the motion characteristics of tissue-mimicking phantoms from ultrasound B-scans, by A. Brasher, D. K. Nassiri and A. E. A. Joseph

Systems for evaluating the clinical potential of speckle suppression and parametric imaging, by J. C. Bamber, J. V. Phelps, G. Cook-Martin and C. R. Hill

The application of knowledge-based techniques to the interpretation of ultrasound images, by A. S. Morton, G. Winstanley and R. J. Burwood

A large-capacity, low-cost image archiving system using a personal computer and optical disk, by A. Parkin, H. M. Norwood and A. J. Hall

Recent developments in the NPL ultrasound beam calibrator, by A. Shaw and R. C. Preston

The enhancement of cavitation effects by acoustic pulsing and by a relative rotation of the sample and the beam

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When sound cavitates a liquid, sonoluminescence can occur. This luminescence originates from the reaction of free radicals created within collapsing bubbles. Thus the production of sonoluminescence indicates the presence of free radicals, and therefore the potential for biological damage. Previous workers have increased biological damage and chemical effects due to ultrasound by acoustic pulsing (Hill et al. 1969) and by rotating biological samples in an ultrasound beam (Church & Miller, 1983). Sonoluminescence has also been enhanced by pulsing (Pickworth et al. 1988) and by rotating (Leighton et al. 1988) a therapeutic ultrasound beam. In both the pulsing and the rotating acoustic regimes, bubbles that were originally non-oscillating are forced into oscillation. Computer plots show that before the steady-state motion is reached, transients in the function can cause the minimum bubble volume attained in an oscillation to be greatly reduced, consequently increasing the maximum temperature and pressure generated within the bubble. This would enhance the free-radical production, and so increase the likelihood of biological damage. It is proposed that this transient excitation of bubbles contributes to the effects outlined above. This theory is supported experimentally by the

detection of short-lived flashes of sonoluminescence at the start of continuous-wave insonation, and at the beginning of each pulse during pulsing. High-speed photography can also be used to verify the predictions of the computer plots.

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The search for free-radical production in the ultrasonic beam produced by duplex ultrasound systems

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Duplex ultrasound equipment is now widely used in paediatric and adult investigations, particularly in cardiology. The higher acoustic output levels obtainable in pulsed Doppler mode currently restricts its use in fetal examinations. Theoretical studies indicate that cavitation effects may be generated by high-intensity microsecond pulses of ultrasound. The high temperatures and pressures produced within a collapsing or oscillating bubble in an ultrasonic field can produce free radicals and visible light is emitted from the gas within the bubble. The light generated in this manner is called sonoluminescence. Under certain conditions, sonoluminescence can be detected with the naked eye when water is insonated by physiotherapy ultrasound equipment. To extend our knowledge of biological effects arising from the use of commercially available diagnostic ultrasound equipment, sonoluminescence and free-radical production have been studied. Sensitive photon detection equipment has confirmed sonoluminescence production in the ultrasonic field of physiotherapy equipment at the output levels greater than 1 W/cm. A Hewlett Packard 77020 phased array duplex system (2.5, 3.5 and 5 MHz transducers) and Ultramark 4 ultrasound equipment (3 and 5 MHz transducers) have therefore been evaluated. All ultrasound equipment control parameters have been selected to maximize the peak negative pressure in the ultrasonic beam. In each acoustic field the photon count obtained during ultrasonic irradiation was compared with that measured when power was disconnected to the transducer. Using a terephthalic acid dosimeter the free-radical concentration has been assessed. Sonoluminescence was not detected and the paired photon counts never exceeded that attributable to random (N) fluctuations (typically 1%). Free-radical production could not be detected using the terephthalic dosimeter.

Wound healing acceleration by ultrasound

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Ultrasound increases the rate of tissue repair after injury. However, the mechanisms involved in this are not yet fully understood. With the objective of contributing to the elucidation of these mechanisms, the effects of therapeutic ultrasound at two different dosages on the repair of full-thickness skin lesions have been tested. The effects were compared with those in sham-insonated controls at 5 days after injury. Treatments were given on Days 0, 1, 2, 3 and 4, i.e. in the inflammatory and early proliferative phases of repair. The treatment regimes used were either 0.1 W/cm² continuous ultrasound or 1:4 pulsed ultrasound with a "temporal peak" (pulse average) intensity of 0.5 W/cm². The temporal average intensity was therefore kept constant at 0.1 W/cm². In both regimes the frequency used was 3 MHz; ultrasound was applied for 5 min daily. It was expected that the use of the same temporal average intensity in the two regimes would produce similar thermal changes in the tissues irradiated and that they would be below a physiologically significant level. However,

the higher peak intensities in the pulsed treatments were expected to affect the incidence of cavitation and acoustic microstreaming differentially. The criteria used for quantification of wound healing were angiogenesis and changes in the differential cellularity of the wound beds. The results obtained confirmed that low-intensity ultrasound stimulates repair and demonstrated that this stimulation includes an increase in angiogenesis. There was also a decrease in the number of inflammatory phase cells (polymorphonuclear leukocytes and macrophages) and an increase in the number of proliferative phase cells (fibroblasts and endothelial cells). Since the levels of ultrasound used were too low to produce a therapeutically useful temperature increase, predominantly nonthermal effects, e.g. stable cavitation and/or acoustic microstreaming, must be involved. Intensities (spatial average, temporal average) as low as 0.1 W/cm² can stimulate tissue repair.

Absence of sonoluminescence in the human cheek

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When a bubble in a liquid is subjected to the pressure wave produced by an ultrasound field, it will undergo radial oscillations. If the ultrasound is of sufficiently high power, bubbles may collapse adiabatically at the point of maximum pressure in the cycle. This is known as transient cavitation. Very high temperatures (1000s K) are reached and molecules of gas or vapour in the bubble may break up into free radicals, which on recombination emit visible light, known as sonoluminescence (SL). The conditions that give rise to cavitation and SL should be avoided in the clinical use of ultrasound, because of the high temperatures and free radicals produced. An attempt was made to look directly for evidence of SL in the human cheek by placing a physiotherapy transducer on the outside of the cheek and a light guide, leading to a photomultiplier, on the inside of the cheek. A photon counter was used to count the pulses of SL received by the photomultiplier. The maximum intensity (spatial average) at which experiments were performed was that at which subjects just began to feel pain. This was 2 W/cm². With continuous-wave ultrasound of up to 2 W/cm², no SL was detected from the cheek. A simple theoretical analysis of the collection efficiency of SL by the light guide was performed. From this, and from data obtained from subsidiary experiments, a calculation was performed to show that the amount of SL produced in the cheek on exposure to therapeutic ultrasound is less than 1/200th of the amount of SL produced in the equivalent volume of water.

The potential of seismic migration for medical ultrasound image enhancement

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Present-day medical ultrasound techniques are indispensable in many fields of medicine, in particular obstetrics and cardiology. Substantial advances in diagnosis have resulted from improvements in spatial resolution, achieved by beam-width reduction using techniques such as focusing and aperture synthesis. As the limit of these techniques is approached, further enhancement of the image is possible only by employing

some form of post-acquisition data processing, such as migration. Migration is an image enhancement technique that is used during the processing of seismic exploration data. Specifically, it removes, in some optimum sense, the propagation effects of the sub-surface and places reflectors at their correct geological positions and collapses diffractions. All migration techniques are based on the acoustic wave-equation, and involve a two-step process, downward continuation followed by an imaging step. Since the imaging step is fairly trivial, most migration algorithms differ from each other in their approach to wavefield extrapolation, the complexity of which depends largely on the migration velocity function. Also, it should be noted that migration may be carried out in either a 2-D or 3-D sense. This paper reviews the major migration methods currently used in the seismic exploration industry, and illustrates them with typical examples. The potential of the technique for enhancing medical ultrasound images is then indicated, and the major differences between application of the technique in the two different fields is discussed. Finally, some practical aspects regarding the implementation of migration algorithms for medical ultrasound are given, and the paper concludes with a short discussion of 3-D migration techniques, again with reference to applications in medical ultrasound.

Determining the motion characteristics of tissue-mimicking phantoms from ultrasound B-scans

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This paper describes research into computerized analysis of ultrasound images with the aim of extracting parameters relating to the motion of soft tissue from the images. An algorithm based on the technique described by Dickinson and Hill (1982) has been developed, which involves calculating the correlation coefficient between successive frames at many positions within the B-scan. Several parameters are then calculated from the variation of the correlation coefficient with time for each position, and hence the spatial variation of these parameters may be displayed. In particular, a method to determine a parameter whose value depends on the elasticity of the material being scanned is assessed, using tissue-mimicking phantoms "wobbling" in response to a controllable mechanical source of motion. The additional problems of applying this method in a clinical situation are discussed.

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Systems for evaluating the clinical potential of speckle suppression and parametric imaging

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We have previously described methods of processing echographic images that use multivariate statistical techniques to recognize (a) the speckle signature of a particular scanner and (b) the image textural characteristics of specific tissue classes. The former of these is used for B-scan image improvement by adaptively smoothing the speckle. The latter

enables the display of new images based on textural similarity, such as the probability of belonging to a particular class of tissue. Two systems have been constructed as to provide fast on-line results, as a means of evaluating the performance and application of these techniques in a clinical setting. The feasibility of real-time performance of two-dimensional processing was successfully demonstrated using an analogue hardware implementation of a simplified speckle reduction algorithm. A video tape is shown to illustrate the results and some of the problems that arise with this approach. To complement this, a slower but more versatile and accurate system was constructed around a commercially available image processor. Whole images may be processed in 15 to 30 s or specified regions, if small enough, may be processed at rates approaching real-time. The operator may select one of a number of processing algorithms, all implemented in SIMD (single instruction multiple data) form. These include a method of textural parametric imaging that combines two uncorrelated measures of image texture with the speckle-reduced echo image using primary hue addition.

The application of knowledge-based techniques to the interpretation of ultrasound images

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Interpretation of ultrasound images is a difficult process for an untrained observer. Computer interpretation of such images presents its own unique set of problems. A current research project within the Artificial Intelligence Laboratory of the Information Technology Research Institute is concerned with the development of a computer system able to interpret images of the gallbladder region of the human liver. Expert system technology appeared to provide the most viable approach for dealing with this anatomical interpretation process. The diversity of information and the complex inter-relations apparent in the spatially related data were found to demand the kind of capabilities afforded by an essentially declarative system capable of exploiting heuristics. In carrying out early development work, it was found that the actual representation of anatomical and pathological knowledge posed the most significant problems. Interpretation cannot begin until a true representation of the image has been given to the expert system. Hence, current work has involved the design of a realistic, high-level image description protocol (IDP), the design philosophy being to develop a minimum set of general descriptors so as to make the IDP as flexible as possible. Developing such a protocol is an iterative process and the true test of its descriptive power lies in its ability to describe a multiplicity of images. The current protocol has been tested on two vastly different gallbladder images and at this stage it appears capable of adequately describing more. The next stage in the testing of the adequacy of this protocol will arise as the interpreting expert system, with ability to intelligently reason about this high-level data, is developed.

A large-capacity, low-cost image archiving system using a personal computer and optical disk

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Diagnostic imaging departments generate large amounts of image data from a variety of sources (ultrasound, nuclear medicine, CT, MRI, digital radiography). Long-term storage of these images requires a low-cost, large-capacity archiving system. Floppy disk storage, which is often provided by the manufacturer for long-term storage of images, suffers from relatively high cost, a small number of images per disk and occupies a large amount of floor space. Optical disks have recently become available for use with industry-compatible personal computers. They offer the benefits of large capacity (typically 800 MBytes), fast data-access time, are cheaper than floppy disks (by a factor of ~20) and are much more compact. Transfer of data between the imaging device and optical disk poses problems as direct interfacing of the optical disk's personal computer to the imaging device is not usually possible since this may invalidate the manufacturer's warranty. The alternative approach of decoding the floppy disks generated by the imaging device is difficult, particularly if details of image storage format are not available. Our solution is to use the personal computer interfaced to a floppy disk reader to detect the beginning of a file marker on the floppy disk from the imaging device. A sector-by-sector copy of this data is made onto the optical disk (without decoding) and the operator enters details of the file, including patient name, date and patient identifier, onto a conventional database which is held on hard disk. The database generates a reference pointer through which the file can be located. To retrieve the data the patient's name and identifier are entered and the file is located and loaded into memory. It is then copied back onto floppy disk in the same format in which it was read. The disk can then be used at the viewing console of the imaging device. A detailed description of the system hardware and software is presented together with the operational procedure.

Recent developments in the NPL ultrasound beam calibrator

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Until the commercial launch of the NPL ultrasound beam calibrator (UBC) 3 years ago, the full characterization of ultrasonic scanners was restricted to a few specialized laboratories. With the current UBC it is possible to assess rapidly, on site, a wide range of relevant acoustic parameters for scanners operating in any of the discrete or combined modes. The system consists of a multi-element membrane hydrophone linked to a microprocessor-based data acquisition and display system, and is traceable to national standards. A new programme of research and development is in progress to produce the next generation of UBCs. Some of the important features that will be introduced are automatic recording of transducer-to-hydrophone separation, averaging routines, fast Fourier transforms, correlation for spatial-averaging and bandwidth limitations, calculation of uncertainties, and improved data storage; in addition, the research programme aims to enhance the initial configuration of the UBC to even the most complex modern scanners. The new system will not only be easier to use, but it will also be an important step towards the calculation of *in situ* exposure levels. Eventually it may be possible to derive biophysical end-points such as temperature rise using realistic propagation models. These developments will also be valuable to manufacturers, helping them to optimize performance and to produce better equipment. A report of progress in the development and implementation of the new features is given and their relevance to the assessment of safety and performance discussed.

Gynaecological ultrasound

Chairmen: Dr D. H. A. Redford and Dr M. P. R. Hamilton

Vaginal ultrasound in infertility and early pregnancy, by R. K. Goswamy

Transvaginal colour flow Doppler studies of the uterine arteries, by C. Steer, S. Campbell, B. A. Mason and J. Pampiglione

A reproducibility study for Doppler ultrasound in the non-pregnant pelvis, by C. M. Farquhar, T. Rae, J. Wadsworth and R. W. Beard

Ultrasound can reliably detect the polycystic ovary: a simple method for establishing an ovarian scanning service, by J. A. Eden and J. Place

Is there a place for per vulval ultrasound scanning in non-sexually-active gynaecology patients with oligomenorrhoea or amenorrhoea? by M. J. O'Dowd

The improved diagnosis and subsequent management of tubal abortion as a result of vaginal sonography, by D. E. Robertson, B. Smith and I. Craft

Assessment of cervical tumour volume by combined transvaginal and transrectal endosonography, by J. Browning, E. Whipp and M. Halliwell

Vaginal ultrasound in infertility and early pregnancy

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When real-time mechanical sector ultrasound became available in 1980 it was hailed as a major breakthrough for gynaecological ultrasound. However, in 1986 Feichtinger and Kemeter described the use of a mechanical sector probe used vaginally for oocyte recovery in *in vitro* fertilization. At Bourn Hall we

started using a vaginal probe in February 1986 to monitor follicular growth during the ovarian cycle. In an initial pilot study performed on patients attending for frozen embryo replacement, all patients were scanned abdominally and again vaginally by an observer unaware of the abdominal results. It soon became evident that vaginal ultrasound was far superior to abdominal ultrasound in that imaging was clearer, patient acceptance was extremely high, and diagnosis was accurately performed in all cases. Sixty-five percent of women preferred

vaginal scanning to the abdominal route mainly because there was no need to fill the bladder. A further 30% remarked that they were equally happy with both techniques whereas only 5% preferred the abdominal route. The main reason for preferring the abdominal route was to avoid the embarrassment of vaginal scanning. Since that time more than 2000 patients have been scanned vaginally and the percentages have remained remarkably similar. By May 1986 we started performing vaginal ultrasound for oocyte recovery and soon discovered that the oocyte recovery rate per patient was greater than 7 and that the oocyte recovery rate per follicle aspirated was greater than 95%. To date, more than 1500 women have been scanned vaginally for oocyte recovery and 95% of all oocyte recoveries at Bourn Hall are now performed using this route. The only indication for laparoscopy is GIFT (Gamete Intra Fallopian Transfer). The use of vaginal ultrasound in the diagnosis of early pregnancy and its complications is now routinely practised and in all cases of vaginal bleeding or pain in pregnancy, vaginal ultrasound has been shown to make the diagnosis at an earlier stage. A fetal heart beat is demonstrable by Day 20 post-ovulation and a yolk sac is demonstrable by Day 28 post-ovulation. In our experience, 10% of all pregnancies achieved by *in vitro* fertilisation are noted to have low β -HCG levels during the early developmental stages and vaginal ultrasound has proved invaluable in differentiating between blighted ova, retro-implantation bleeds and ectopic pregnancies. Blighted ova have been correctly diagnosed in 33 cases as early as Day 25 post-oocyte-recovery. The diagnosis of retro-implantation bleeding was made on the basis of low HCG levels and fluid collection between the implantation site and the uterine wall. We have confirmed the diagnosis in 12 such cases and 50% of these cases have subsequently had ongoing pregnancies and/or delivered live infants. Of the other 50%, four were noted to stop growing 2 weeks after the first scan and the other two stopped growing within a week of the first scan. The prognostic value of diagnosing retro-implantation bleed makes it easier to advise patients in these situations. The use of vaginal ultrasound in the diagnosis and management of ectopic pregnancy has now been routine for the last 2 years. The first sign of the possibility of an ectopic pregnancy developing is a drop in the progesterone levels on Day 12 post-oocyte-recovery followed by a low rise from Day 15 onwards. Beta-HCG levels in these cases are consistently depressed and at ultrasound examination on Day 25 it is possible to diagnose an ectopic pregnancy. The main advantage of vaginal ultrasound over abdominal ultrasound is that there are no intervening loops of bowel between the transducer and the fallopian tubes and therefore this diagnosis can be made with certainty. Embryonic echoes can be identified positively from Day 25 post-oocyte-recovery onwards. Out of 32 cases of ectopic pregnancy diagnosed in the last 2 years, 15 were noted to be anembryonic. The HCG levels in these cases did not rise as high as expected and there was spontaneous resorption over a period of 6–8 weeks. In one case the HCG levels continued to double every 3–5 days and the injection of methotrexate using vaginal ultrasound-guided needling was performed. In three cases, injection of potassium chloride, using the same needling technique, was performed because a fetal heart beat was positively identified in the ectopic fetus. All these cases have resolved subsequently. In one case of triplet pregnancy the patient was noted to have two intrauterine sacs and one ectopic sac. An embryonic echo was identified in the ectopic sac but there was no fetal heart beat. This ectopic resolved spontaneously. In nine cases a fetal heart beat was positively identified and laparoscopic salpingectomy was performed so that the patients could be discharged within 48 h. In three cases a fetal heart was identified in the ectopic pregnancy and the

tubes were inaccessible for laparoscopic removal and therefore laparotomy had to be performed. It is our opinion that most ectopics can be managed conservatively if they are diagnosed prior to tubal rupture. This warrants further evaluation.

Transvaginal colour flow Doppler studies of the uterine arteries

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A potential cause of decreased fertility that has not been amenable to diagnosis until recently is that of an altered uterine blood flow outside the normal range. To date, flow has been assessed by means of Doppler duplex systems via an abdominal scan. Transvaginal ultrasonography with colour flow Doppler has the advantage that it does not require a full bladder and permits close proximity, with a low angle to the uterine artery, which can be identified with certainty. The result is superior waveforms for analysis of impedance. Results of colour flow mapping of the uterine arteries are presented, using the Diasonics Vingmed CFM 700, a scanner with 7.5 MHz ultrasound and 6 MHz colour pulsed Doppler. Initial work has shown that the pulsatility index (PI) decreases with the increasing plasma oestrogens during the menstrual cycle. The normal range of PIs for cycling woman undergoing insemination with donor sperm is presented. The correlation of PI with levels of serum oestradiol and progesterone is shown.

A reproducibility study for Doppler ultrasound in the non-pregnant pelvis

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A study of Doppler ultrasound signals from the uterine and ovarian arteries in non-pregnant women was conducted to determine the feasibility of obtaining reliable recordings from these sites. Eleven healthy volunteers who were not on hormonal contraception were studied a minimum of five times during a menstrual cycle. The ultrasound scans were performed by two observers usually immediately after each other. Ultrasound measurements were taken of the uterine length, uterine depth, the endometrium and the ovarian follicle. Doppler signals were collected from the ovarian and uterine arteries and the pulsatility indices (PI) calculated. The results show that the ultrasound measurements of pelvic organs were reproducible and the maximum coefficient of variation was 9% between observers. However, the differences between observers for PI were considerably higher and the maximum coefficient of variation was 37% for the ovarian artery. When the observations were repeated immediately by the same observer the coefficient of variation was 9%, but 30 min later it was almost 60%. In view of these results it would seem that studies using Doppler signals in the non-pregnant pelvis are as yet unreliable.

Ultrasound can reliably detect the polycystic ovary: a simple method of establishing an ovarian scanning service

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Ovarian scanning to monitor ovulation induction therapy and to classify ovarian morphology has been performed successfully at Charing Cross Hospital using the transabdominal, full bladder technique and our obstetric scanner (Hitachi EUB 340 with a 3.5 MHz curvilinear transducer and a long focus). During an initial "learning" phase, sonographers were referred cases of laparoscopy-proven polycystic ovary (PCO), with the classical signs and biochemical profile of PCO syndrome. The second phase involved a "blind" comparison of an ultrasound diagnosis of PCO with laparoscopy as the "gold-standard", where it was found that these two techniques agreed 91% of the time (Eden, 1988). The third phase was a prospective study, using ultrasound as the "gold standard", to examine the consequences of an ultrasound diagnosis of PCO. One hundred consecutive cases of ultrasound-diagnosed PCO were compared with 77 ovulatory controls with sonographically normal ovaries. A normal range for the early follicular phase had been established using 140 ovulatory women with laparoscopically normal ovaries. In the PCO group, 26 were hirsute, 51 were oligomenorrhoeic, 30 were obese (body mass index $>25 \text{ kg/m}^2$) but 33 were neither obese, hirsute nor oligomenorrhoeic. Ninety-one had at least one abnormal blood test to support the diagnosis of PCO, compared with 8% of the controls ($p < 0.001$). The volume of the PCO was significantly correlated with serum luteinizing hormone (LH), testosterone (T) and negatively correlated with serum prolactin (PRL). Biochemical normal ranges must be based on women with normal ovaries. We were able to lower the upper limit of normal for LH from 15 to 9.8 U/l. Scanning and blood collection should be performed in the early follicular phase. Late follicular scans may have ovarian morphology obscured by a pre-ovulatory follicle and LH and T surge during this time. Luteal phase blood samples may have suppressed levels of LH. The reliable ultrasound diagnosis of PCO requires a simple, staged approach. Ultrasound staff should be able to gain confidence by scanning proven cases of PCO. Early follicular phase biochemical profiles including LH, T and sex-hormone binding globulin will usually agree with an ultrasound diagnosis of PCO.

Reference

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Is there a place for per vulval ultrasound scanning in non-sexually-active gynaecology patients with oligomenorrhoea or amenorrhoea?

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Ultrasound has a large part to play in the diagnosis and management of patients with oligo- and amenorrhoea. An abdominally performed pelvic ultrasound is not always technically rewarding, and it may be difficult or impossible to visualize one or both ovaries. A number of patients concerned will be non-sexually-active teenagers in whom intravaginal

ultrasound is not desirable. A trial of per vulval ultrasound was used in a number of sexually-active patients to visualize pelvic structures. The technique was compared with intravaginal and abdominal ultrasound in the same patients and pictorial records compared. The results and conclusions are outlined.

The improved diagnosis and subsequent management of tubal abortion as a result of vaginal sonography

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Developments in instrumentation and improvements in scanning techniques enable screening of live tubal and cornual pregnancies from 3 to 4 weeks gestation onwards. The detection of tubal abortion remains difficult by conventional transabdominal scanning, especially in the absence of an intact amniotic sac. Vaginal sonography not only provides an effective means of diagnosing this condition but also the ability to assess the continued growth or regression of subsequent tubal mole formation. During the past 18 months, 17 live ectopics and 19 cases of tubal abortion have been diagnosed within the above unit. A collapsed sac and/or mass of persistent trophoblastic tissue was missed or poorly visualized by transabdominal scanning in nine of the cases of tubal abortion. The excellent tissue information provided by vaginal scanning allowed recognition of either proliferating or regressing trophoblastic/decidual tissue in all cases of tubal abortion. Of the 19 cases, the tubal lesion was shown to be regressing in 14. These were treated conservatively and progress was monitored by serial vaginal ultrasound. In the remaining cases, the formation and continued growth of a tubal mole with evidence of haemorrhage was confirmed and surgical intervention indicated. Vaginal scanning has a major role to play in the early detection of ectopic pregnancy and, in particular, tubal abortion. It allows a more effective means of patient management, following both assisted reproduction techniques or natural conception, as well as providing accurate post-operative assessment in cases of ultrasonically-guided reduction of ectopic pregnancy.

Assessment of cervical tumour volume by combined transvaginal and transrectal endosonography

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Cervical cancer is common and its incidence is increasing. It is increasingly realized that prognosis is related to tumour volume at presentation and that radiotherapy may be tailored to the size and site of tumour. A combined transvaginal and transrectal endosonographic approach allows three-dimensional measurement of tumour bulk. The patients had micturated between 1 and 2 h previously and were anaesthetized. A Bruel and Kjaer 1846 module was employed. In the supine position, with flexed and abducted hips, the patient underwent transvaginal scanning: using a Bruel Kjaer 8537 7 MHz offset sector scanner, the cervix, uterus, bladder and pelvic small bowel are visualized. A sagittal image gives two diameter measurements of the cervical tumour (designated *a* and *b*) which is measured and photographically recorded. The patient then turns to the left lateral position. A Bruel and Kjaer 1850 probe with 5.5 MHz radial transducer is passed rectally, and the cervix and parametrium visualized anteriorly. From

this transverse section, diameters b and c are recorded. The tumour volume (V) is deduced as: $a \times b \times c = V \text{ cm}^3$. Thirty-two patients with cervical cancer had been assessed. There is good correlation with volume of surgically resected specimens. A correlation of stage with volume is represented diagrammatically. In conclusion, combined transvaginal and

transrectal endosonography provide an accurate method of assessment of local tumour extent and volume. Radiotherapy planning may be modified according to tumour bulk and size of spread. Tumour volume is a good likely prognostic indicator of lymph node metastasis and patient outcome.

Ultrasound of superficial structures and endosonography

Chairmen: Dr A. P. Bayliss and Dr G. R. Sutherland

The spectrum of echographic appearances of the thyroid, by C. Metreweli

The ultrasound of thyrotoxicosis, by I. W. J. Birchall, C. C. Chow, C. Cockram and C. Metreweli

The role of ultrasound in the detection of non-radio-opaque foreign bodies, by R. S. D. Campbell, F. J. Gilbert and A. P. Bayliss

Ultrasound changes following endoscopic laser coagulation of localized cancer of the prostate gland, by C. Charig, T. McNicholas, S. St. C. Carter and E. P. N. O'Donoghue

A dual-transducer scanner for rectal imaging, by S. D. Pye, W. N. McDicken, S. R. Wild and T. Loupas

Ultrasound and computed tomography in the diagnosis of masses of the parotid gland, by C. Metreweli, W. King and L. Kreef

Foot shape analysis by ultrasound, by W. Macdonald, M. A. Bradley and A. Mowat

Ultrasound characterization of breast tissue, by P. D. Edmonds, C. L. Mortensen and P. Schattner

Colour Doppler in breast diseases, by D. O Cosgrove and J. C. Bamber

The spectrum of echographic appearances of the thyroid

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The imaging of thyroid diseases poses apparently insurmountable problems at this moment in time. Thyroid diseases are poorly understood. Many decades of histopathology and two decades of sophisticated immunology have not shed any light on aetiology. This can be seen in the limited treatments available, which simply either interfere with thyroid biochemical function or ablate thyroid tissue (surgery or radioactivity) or replace missing thyroxine. There are no treatments that attack the root cause of the disease. Furthermore, the imaging diagnosis of thyroid malignancy is hampered by the fact that the presence of early carcinoma can only be excluded by histological demonstration of microscopic vascular invasion. For some time the mainstay of thyroid imaging has been scintigraphy, a technique whose harmlessness is almost matched by its uselessness. Ultrasound had been little better because appearances have been related to clinical diagnoses, a technique valid with other organs but which must fail when there is already chronic clinical confusion. In order to clarify the potential value of ultrasound, a classification of echographic appearances needs to be established. Following this the clinical problems related to each appearance can be studied in the hope that hitherto unappreciated patterns may emerge. This may give some insight into thyroid disease, and indicate the role, if any, of imaging in thyroid disorders. This classification is based on examination of over 2000 thyroid problems and a smaller number of asymptomatic volunteers. Features that have not been found to be of sufficient differentiating value such as haloes and calcification have been demoted and the classification depends mainly on echotexture of the parenchyma and discrete thyroid masses. The result is some 30 identifiable patterns (type number in parentheses).

The parenchyma may be fine textured and bright (1), medium (2), or coarse (3); greater changes in amplitude result in spotty thyroids (4), confluent spots (5), geographic hypoechogenic areas (6), focal hypoechogenic areas (7),

(these are sometimes difficult to distinguish from mass lesions (15) below). Uniformly echo-poor but transonic parenchyma can be "dark" thyroid (8), "dark shadowing" thyroid (9), "dark and streaky" (10) or "grainy" (early multinodular) (11). Homogeneous masses can be anechoic with enhancement and without a wall (12), with a wall (13) or without enhancement (14), hypoechogenic (15), isoechogenic with or without a halo (16,17) and hyperechogenic with or without a halo (18,19). Heterogeneous masses can be echo-poor and walled (20), without a wall (21), contain low echoes with (22) or without (23) cystic areas, isoechogenic with (24) or without (25) cystic areas of hyperechogenic with (26) or without (27) cystic areas. Furthermore, multiple masses may be of uniform (28) or mixed pattern (29) or completely replacing the thyroid (30) (a variant of 11).

The ultrasound of thyrotoxicosis

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Hyperthyroidism is a common condition in the UK, with a community prevalence of 19 out of 1000 women. Graves' disease, toxic multinodular goitre, thyroid adenoma, and the thyroiditides are the commonest causes. Only in Graves' disease and the thyroiditides can remission be anticipated. Ultrasound of the thyroid may allow rapid differentiation of these disease processes that show characteristic parenchymal patterns. Rational selection of appropriate treatment (antithyroid drugs or radioiodine/surgery) can then be made. The appearances on ultrasound of the thyroid of 392 Cantonese patients presenting with a clinical diagnosis of thyrotoxicosis have been reviewed. Twenty-four were subsequently found to be euthyroid. Of the remainder, 107 had eye or skin signs of incontrovertible Graves' disease. These appearances were

compared with those of 50 healthy Cantonese volunteer controls. Fifty-three (49.5%) of patients with incontrovertible Graves' and 118 (45.2%) of thyrotoxic patients without eye/skin changes showed multiple hypoechoic "spots" within their parenchyma, a pattern not encountered in euthyroid patients nor controls. Two patients showed sonographic evidence of subacute thyroiditis and 13 had features of Hashimoto's thyroiditis. Patients with "Hashi-toxicosis" should be treated cautiously with antithyroid agents, and those with subacute thyroiditis with anti-inflammatory agents. Radioiodine and surgery should be avoided. Those remaining thyrotoxic patients with eye signs and those without eye signs or nodules may be treated initially with antithyroid agents with reasonable hope of success. Scintigraphy will still be necessary to distinguish which of the remaining 12% of thyrotoxics have Graves' disease and coincidental nodular disease treatable with antithyroid drugs, from those with hyperactive nodular disease meriting radioiodine/surgery.

The role of ultrasound in the detection of non-radio-opaque foreign bodies

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The detection and localization of non-radio-opaque foreign bodies in soft tissues is a recurrent problem in the Accident and Emergency department, often resulting in lengthy and unfruitful exploratory procedures. While ultrasound is an accepted mode of imaging of muscles, tendons and soft tissue, there are few reports of detection of foreign bodies in soft tissues, although its application in ocular trauma is well recognized. While it has been shown that ultrasound may be used in the detection of foreign bodies, the reliability of the examination is not known. In this study, 50 consecutive referrals for suspected non-radio-opaque foreign bodies in distal extremities were reviewed. Examinations were performed with a real-time, high-resolution 10 MHz sector scanner (Diasonics DRF 400) with a lateral resolution of 1–2 mm and an axial resolution of 0.2 mm. From the initial 50 patients referred, 22 had foreign bodies removed at operation (18 wood, two thorn, two glass) of which ultrasound detected 21. There were three false positive examinations. The remaining patients all had negative ultrasound scans, and these were considered as true negatives, since there was either a confirmatory negative exploration or the patients were followed-up until clinical remission of symptoms. The sensitivity was 95%, specificity 89% and the predictive value 87%. This paper presents a more detailed analysis of the results obtained, together with a discussion of the typical ultrasound appearances, causes of misinterpretation and some pitfalls that may be encountered. In conclusion, the study demonstrates not only that ultrasound is a safe, reliable method of detection of non-radio-opaque foreign bodies, but is also of use in determining the exact location of these foreign bodies and is extremely valuable in patient management.

Ultrasound changes following endoscopic laser coagulation of localized cancer of the prostate gland

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We have used radical endoscopic resection of the prostate gland in combination with NdYAG laser coagulation for the control

of localized prostatic cancer (TOB–T2, NX MO). The patients have been closely followed-up with clinical and endoscopic examination, transrectal ultrasound and biopsy, and serum PA measurements. We describe the characteristic ultrasound changes seen after laser therapy and show that this is the best means of monitoring local therapy. Since April 1986, 20 patients have been treated, of which four had positive biopsies and have been retreated. All the patients now have negative histology, with no signs of local or distant progression. The most striking feature on ultrasound is the marked shrinkage of the gland 3 months after laser coagulation (mean volume 8.1 ml, range 2.3–15.4 ml) compared with pre-coagulation volumes (12.6 ml, range 9.4–19.5 ml), as measured by transrectal ultrasound. This was confirmed by endoscopic and clinical findings. Following radical transurethral resection of the prostate, the volumes fell by 60%, from a mean volume of 31.5 ml (19–46 ml) pre-treatment, to a volume of 12.6 ml (9.4–9.5 ml). At 3 months following laser coagulation, there had been a further reduction of 36% in prostatic volume. This indicates an overall reduction of 75% in glandular volume using this combination therapy. The post-laser appearances are of a short, rounded, dense gland, within which most of the normal architecture has been replaced by areas of high echogenicity, indicative of fibrosis.

A dual-transducer scanner for rectal imaging

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Endoluminal ultrasound of the rectum may allow accurate pre-operative staging of rectal cancer, and follow-up scans may be useful to detect local recurrence and to assess the effect of radiotherapy. Imaging of rectal tumours requires high-resolution imaging of the thin rectal wall layers at short range and high-quality imaging of tumour masses out to the pelvic wall. A variety of commercial ultrasound probes are available for rectal scanning with frequencies from 4 to 10 MHz. However, these probes normally contain one transducer, operating at one frequency and with a fixed focal range. This is incompatible with high-quality imaging of both the rectal wall and large tumour masses. A probe has therefore been designed containing two back-to-back transducers of frequencies 7.5 and 10 MHz. The transducers rotate around the axis of the probe producing a 360° image of the rectum in cross-section. Scans at different frequencies are carried out sequentially and this has proved to be satisfactory in clinical practice. The 10 MHz transducer has a focal range from 5 to 30 mm and is suitable for imaging the rectal wall at close range. The 7.5 MHz transducer has a focal range from 20 to 55 mm and is suitable for imaging tumour masses. Other aspects of the probe design that suit it to rectal imaging are described. The imaging capabilities of the probe have been investigated using a versatile test object consisting of layers of plastic film whose separation can be accurately controlled. The test phantom has been used to demonstrate interference artefacts that may occur when imaging closely spaced interfaces. The ultrasound probe has now been applied successfully to 35 patients and examples are shown of the images obtained. A number of the images have been digitized and processed using computer algorithms, which both reduce the noise present in the image and enhance the visibility of the layers. Examples of these images are shown.

Ultrasound and computed tomography in the diagnosis of masses of the parotid gland

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Because of the peculiarities of parotid gland pathologies in their number, variations and behaviour (the benign are not as benign as elsewhere in the body and the malignant are not as malignant), the radiologist is not expected to make a histological diagnosis of a parotid mass. The radiologist's function is to establish for the surgeon the location of a suspected parotid mass. Is it extrinsic? If intrinsic, is it located in the deep or superficial lobe? Is there any spread outside the gland or lymphadenopathy? The practice in our department had been to use computed tomography (CT) sialography to answer these questions. But with the availability of high-quality, high-resolution echography and flexible stand-off gels, echographic imaging of the parotid has become easy and rapid and as reliable as CT. As a result of our experience of over 40 cases, it has now become the imaging investigation of choice. Computed tomography is reserved for special problems such as deep lobe tumours, accessory parotid masses or supplementation of technically unsatisfactory echography.

Foot shape analysis by ultrasound

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As part of a study to determine the mechanics and anatomical effects of metatarsal orthoses, ultrasound "B" scanning was used to measure changes in the forefoot due to metatarsal domes. Ten normals and 16 rheumatoid patients were scanned weightbearing with the foot in a water-bath, scanning vertically over the dorsum of the foot from the first to the fifth metatarsal head. Images were taken using a 5 MHz, 13 mm probe and were recorded with a flat format camera. Dorsal outlines and metatarsal positions were digitized and area, width and height were calculated for each. Analysis of repeatability showed that dorsal area was the most useful parameter, giving statistical significance at the $p < 0.001$ level. Analysis of variance to determine anatomical effects of metatarsal domes yielded between-subject significance at the $p < 0.001$ level, but no significance for dome effects. It is concluded that ultrasound scanning is a useful technique in the analysis of anatomical changes in the forefoot, and the metatarsal domes do not significantly alter the forefoot anatomy.

Ultrasound characterization of breast tissue

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This research aims to determine whether there is a set of ultrasound parameters that are sufficient to discriminate malignant from benign tumours of the human breast and to clarify contradictions in the literature concerning the dependence of ultrasound attenuation on the pathological state of breast tissue. Sound speed is also determined as an important, non-controversial characteristic of pathological state. These data are required for an adequate assessment of

the potential of ultrasound transmission and computed tomographic imaging in breast cancer detection. Freshly excised breast biopsy specimens maintained at 37 °C are interrogated by a finely focused ultrasound beam and the transmitted ultrasound is detected by a phase-insensitive acoustoelectric receiver, thereby eliminating errors due to phase cancellation. Back-scattered ultrasound is collected by the same focused transducer, acting as the receiver, and normalized by means of a plain, stainless steel reflector. Data are obtained for the frequency range 3 to 9 MHz; sound speed is determined by measurement of time of flight, effectively at 6 MHz. Specimens are routinely examined histologically and enlarged photographs of stained sections of the tissues that have been interrogated ultrasonically are made for analysis. Results to date show the expected discrimination between normal and abnormal tissues by sound speed alone, but no such discrimination by sound attenuation alone. More sophisticated discrimination sets will be required to utilize the attenuation alone and to utilize the attenuation data in the clinical contexts of interest. Backscatter data analysis is under development, based on an adaptation of the theory of Madsen et al (1984) to include spectrum analysis of received waveforms instead of digitization of the r.f. signal. (This research is supported by Public Health Service Grant No. CA34398 awarded by the National Cancer Institute, US Department of Health & Human Services.)

Reference

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Colour Doppler in breast diseases

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Distinctive flow signals are obtained from malignant breast tumours using continuous-wave Doppler, but these methods are cumbersome because they are point sensitive. The area interrogation of colour Doppler (CD) flow-mapped systems speeds the study of vascularity because complete tomograms can be assessed rapidly. It also displays the pattern of vascularization. Breast masses in 65 patients were evaluated using the Acuson 3 MHz CD system and the results compared with the final diagnosis obtained by biopsy for the 33 malignancies and by biopsy or clinical follow-up in the remainder. The vascularity was subjectively assessed and the peak average velocity was measured for larger vessels. The video-recorded CD images of the lesions were quantitated using a masking screen to provide a count of the number of vessels and their relationship with the tumour edge. Most malignant tumours > 1 cm in diameter are heavily vascularized, both at the growing edge and within the tumour. Many show high-flow signals, often with distinctive abnormal flow patterns, tentatively attributed to A-V shunts. The flow is roughly proportional to tumour size. Benign masses and regions of dysplasia are relatively poorly vascularized and lack the high flow and abnormal patterns. There is no detectable flow associated with cysts. The striking flow abnormalities in tumour could prove useful in drawing attention to suspicious regions for biopsy, in differential diagnosis and in predicting response to hormones or chemotherapy, especially with the expected improvement in sensitivity when CD systems operating at higher frequencies become available.

Obstetric ultrasound I

Chairman: Dr M. J. Whittle

The use of ultrasound in multiple pregnancy, by J. P. Neilson

The assessment of fetal growth in multiple pregnancy, by M. A. MacLean, A. M. Mathers, E. B. Melrose, R. C. L. Howat, J. J. Walker and J. R. MacKenzie

An inter- and intraobserver variability study comparing a visual analog scale versus amniotic fluid pocket measurements, by A. M. Mathers, D. M. MacNaught, J. J. Walker, A. D. Cameron and J. R. MacKenzie

The relationship between cord gas analysis and umbilical Doppler waveforms, by S. N. Tyrrell

Pregnancy screening by Doppler velocimetry, by K. P. Hanretty, M. H. Primrose, J. P. Neilson and M. J. Whittle

Evidence of redistribution of cardiac output in asymmetrical growth retarded fetuses, by W. Al-Ghazali, M. Chapman, S. Chita and L. D. Allan

Ultrasound assessment of the cervix: the bladder effect, by G. Mason

Vaginal endosonography: a new method for the objective assessment of the pregnant cervix, by M. J. Quinn, B. Farnsworth, D. Bisson and G. M. Stirrat

Umbilical Doppler studies: possible therapy, by B. Trudinger. Abstract not received

What's new in fetal growth measurement? (Toshiba Lecture) by J. C. Hobbins. Abstract not received

The use of ultrasound in multiple pregnancy

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The risk of all major perinatal complications is magnified by multiple pregnancy. Pre-term delivery, fetal growth retardation and malformation, in particular, are responsible for the continuing high rate of fetal loss. The study of multiple pregnancy is not only intrinsically important but also a potentially valuable source of information about perinatal pathology generally. Study necessitates recognition, and diagnosis of multiple pregnancy is one rationale for routine early pregnancy ultrasonography. The increased incidence of malformation makes detailed inspection of fetal anatomy desirable, although difficult human quandaries may be produced by the demonstration of discordant malformation. Ultrasound-guided "selective feticide" may, in some circumstances, be a less undesirable option than other alternatives. The type of placentation can be predicted with substantial accuracy by ultrasound inspection of the dividing membrane during mid pregnancy and this may be of value in certain clinical situations. Among these is suspected twin-twin transfusion syndrome, a still enigmatic condition attributed to unbalanced anastomotic connections in monochorionic placentas. Extreme cases of the syndrome are identifiable by ultrasound imaging of the fetuses. Pre-term labour (incidence up to 50%) is attributed generally to uterine overdistension although this may be an oversimplification. Clinical examination of the cervix does help to predict pre-term labour in twin pregnancies and this information can be obtained with ultrasound, perhaps optimally using a vaginal probe. Growth retardation is common in multiple pregnancies and is particularly difficult to identify clinically. Ultrasound has an important role in monitoring growth and in assessing fetal well-being. We have been unable to identify any consistent difference in the rate of growth when monozygotic pregnancies have been contrasted with dizygotic, or monozygotic/monochorionic pregnancies have been contrasted with monozygotic/dichorionic. This provides further support for the use of singleton standards to assess the growth or size of twins. Doppler ultrasound has been reported as valuable in identifying both small-for-dates twin fetuses and also the twin-twin transfusion syndrome. Our own experience of this new technology has been disappointing. It has not proved useful in detecting small-for-dates twins. It is difficult to understand why

any consistent pattern of blood velocity waveform should be seen in the umbilical arteries in cases of twin-twin transfusion syndrome.

The assessment of fetal growth in multiple pregnancy

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Multiple pregnancy remains a significant cause of perinatal mortality and morbidity. In an effort to centralize the care of these high-risk pregnancies, a Twins Clinic was established in Glasgow Royal Maternity Hospital in 1983. In addition to the clinical measurement of the symphyseal fundal height (SFH) using a centimetre tape, a policy of monitoring these pregnancies with serial ultrasound examinations was introduced. Each pregnancy was scanned at monthly intervals until 28 weeks. Subsequent examinations were performed at 2-3 weekly intervals. Initial examinations were directed at the determination of fetal number, placental site, the number of sacs present, and gestational age assessment. Subsequent examinations were directed towards the determination of fetal position, biparietal diameter (BPD) and abdominal circumference (AC). From these measurements a calculation of fetal weight was derived. The analysis of 130 twin pregnancies is presented. The accuracy of SFH measurement is compared to ultrasound measurement and the actual birth weights. Particular emphasis is made regarding the accuracy of the Jeanty method of fetal weight prediction compared with AC measurements alone and simple plotting of the AC on centile charts. The relevance of diagnosing the presence or absence of a septum is discussed.

An inter- and intraobserver variability study comparing a visual analog scale versus amniotic fluid pocket measurements

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Amniotic fluid volume (AFV) is an important factor in the biophysical assessment of fetal condition. Several different ultrasound techniques of quantitative measurement of this

parameter have been described and there remains debate as to whether one method is superior to another. This study was initiated to determine whether subjective assessment of liquor volume using a visual analog scale compared favourably with actual measurement of liquor pool size. One hundred and four pregnancies referred for ultrasound examination from 28 weeks were studied. Observer 1 measured the depth, width and length of the largest liquor pool. An assessment of the total liquor was made and plotted on a 10 cm scale graded from no liquor to polyhydramnios. The examination was repeated by a second observer who was unaware of the initial results. Within 10 min the initial observer repeated the examination, the previous results remaining unavailable. The analog scale plot was measured from the left edge. Using the Spearman rank test there was a strong correlation (>0.9) in the inter- and intraobserver measurements of depth, width and length pool measurements and in the analog scale assessment of AFV. This suggests that a subjective assessment of AFV is as reproducible as pool measurement.

The relationship between cord gas analysis and umbilical Doppler waveforms

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Continuous-wave Doppler ultrasound of the fetal umbilical artery is increasingly being applied to clinical obstetric practice, both in the management of high-risk pregnancy and as a screening procedure for low-risk pregnancy. Abnormal waveforms are associated with a high fetal and neonatal morbidity and mortality and are thought to be the result rather than the cause of impaired placental perfusion and gas transfer. The accuracy of these umbilical waveforms in the prediction of chronic fetal hypoxia and acidosis has not been specifically quantified. Comparison of percutaneous umbilical vein samples obtained immediately prior to caesarean section with those after delivery has shown the pH level and base excess to be unaltered by anaesthesia and operative delivery. We have investigated the umbilical venous blood gas tensions and acid-base status at caesarean section in relation to the pre-operative umbilical artery waveform. Simple visual inspection to determine the presence or absence of end-diastolic velocities is compared with more precise mathematical expression of the waveform. We present the results of 150 such blood gas estimations from cases with both normal and abnormal waveforms and demonstrate a strong correlation between progressively abnormal umbilical waveforms and worsening hypoxia and acidosis.

Pregnancy screening by Doppler velocimetry

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Doppler waveforms from the uteroplacental and umbilical arteries were studied in 543 unselected women attending an antenatal clinic. Three hundred and fifty-seven women were studied at 26–30 weeks and 395 at 34–36 weeks; 209 women were studied at both gestation periods. Results were not made available to clinicians. There was no difference in outcome of pregnancies between those with normal and abnormal uteroplacental waveforms but birth weights were significantly

lower in those with an abnormal umbilical artery waveform at either gestation. There were no other differences between groups. These findings do not support the introduction of this new technique into clinical practice before randomized controlled trials have shown some benefit.

Evidence of redistribution of cardiac output in asymmetrical growth retarded fetuses

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Thirty-one cases of intrauterine growth retardation were studied by Doppler estimation of the cardiac output from each side of the fetal heart. The purpose of the investigation was to assess haemodynamic changes compared with the normal fetus. In the normal fetus, there is a higher output from the right heart than from the left. The pulmonary artery flow varies (50–70% of the combined cardiac output with a mean of 58%). There were 15 cases of symmetrical type and 16 cases of asymmetrical type according to the ratio of head to abdominal circumference measurement. In the fetuses with symmetrical growth retardation, the distribution of the cardiac output was normal, the mean velocity of blood flow in the pulmonary artery and aorta were similar, as in the normal fetus, and there was a greater calculated output from the right heart than from the left. The right heart flow expressed as a percentage of the combined cardiac output was not statistically significantly different from the normal fetus. In contrast, all the 16 fetuses with asymmetrical growth retardation had higher mean and maximum velocities in the aorta than in the pulmonary artery. The calculated volume flow from each side of the heart showed a greater output from the left than the right heart in 15 cases. The right heart flow expressed as a percentage of the combined cardiac output in this group of fetuses was different from the normal fetus. This difference was statistically significant ($p < 0.01$). These findings are consistent with theories of the redistribution of fetal blood flow, where cerebral blood flow is preferentially "spared" in the fetus where the essentials for growth are limited in availability.

Ultrasound assessment of the cervix: the bladder effect

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Over the last decade an increasing body of research has suggested the value of ultrasound in the diagnosis of cervical incompetence. This diagnosis is often based on a dilated internal os or a short cervical length, both parameters being interdependent. The correct placing of the internal os therefore becomes critical. Taken too high and incompetence will be overdiagnosed, too low and incompetence will be missed. A review of the literature reveals that the internal os has been sited at points that are not only in themselves variable but also dependent on bladder volume. This in part explains why cervical length measurements have been recorded between 0 and 7 cm. With improved ultrasound resolution it is possible to be more precise in the location of the internal os, at a point within the cervical canal. The present study was designed to investigate the effect an alteration in bladder volume had on ultrasound-observed cervical length. Thirty-one patients, in the second trimester of pregnancy, underwent at least three ultrasound scans with varying bladder volumes. On each

occasion the voided volume of urine was recorded. The results indicate a linear increase in cervical length with increasing bladder volume (the slope was statistically significant, $p = < 0.001$). Explanations of why this should occur include compression of the cervix by the bladder and an alteration in the cervical axis from a vertical to a horizontal structure. These results indicate that it is essential to take into account the bladder volume in any cervical length measurement. Cervical lengths can, however, be obtained over a wide range of bladder volumes and it is not feasible to rely on patients stating that they have a full bladder to standardize bladder volume.

Vaginal endosonography: a new method of the objective assessment of the pregnant cervix

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Digital vaginal examination has been the traditional method for the assessment of the pregnant cervix. It is subjective, cannot assess the length of the cervical canal (from internal os to external os) and may be uncomfortable for the woman. Vaginal endosonography (VES) is a new technique that permits the objective assessment of the pregnant cervix. The two techniques have been compared and further studies of the clinical potential of VES are presented. Vaginal

endosonography is performed in the recumbent position with the hips and knees flexed, and the bladder empty. A 7 MHz endoprobe is used in association with an ultrasound scanner (Bruel & Kjaer 1846). Observer variation was assessed between two independent observers (M.Q. & D.B.) by consecutive scans of the same patient without knowledge of the preceding result ($r = 0.90$). A series of investigations has been carried out in order to assess the dimensions of the pregnant cervix in relation to: (1) primigravid and multigravid women at 12–16 weeks, (2) a comparison of the Bishop score (digital examination) and VES, (3) cervical incompetence and the placement of cervical sutures, and (4) a comparison of the patient acceptance of the two techniques. Results showed that the mean length of the pregnant cervix at 12–16 weeks in primigravid women was 42 mm as opposed to 40 mm in parous women. There is an inverse relationship between the length of the cervical canal as determined by endosonography and the Bishop score by digital vaginal examination. Cervical cerclage at 12–14 weeks does not alter the existing conformation of the internal os as no suture was placed closer than 1 cm from the os. Forty-eight out of 50 women expressed a preference for VES over digital vaginal examination when assessed consecutively by both techniques. In conclusion, vaginal endosonography is a new technique for the assessment of the pregnant cervix. The technique is reproducible and has been preferred to digital vaginal examination by a majority of pregnant women. Vaginal endosonography has considerable potential in a range of common clinical situations in pregnancy.

Obstetric ultrasound II

Chairmen: Prof J. C. Hobbins and Prof. C. R. Whitfield

Ultrasound of the fetal abdomen, by C. Hayward

Post-abortion fetal assessment using ultrasound and radiology, by A. J. Jones, H. S. Andrews and M. Jenkins

Fetal diaphragmatic hernia: the value of fetal echocardiography in predicting neonatal outcome, by D. C. Crawford, V. M. Wright, D. P. Drake and L. D. Allan

The morbidity and mortality associated with an ante-natal diagnosis of bilateral fetal uropathy, by R. J. Arthur, H. C. Irving, D. F. M. Thomas and J. K. Watters

Cardiac scanning at 13–15 weeks gestation, by S. K. Chita, G. K. Sharland and L. D. Allan

Ultrasound of the fetal abdomen

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As the development of antenatal ultrasound has progressed, papers and presentations have tended to concentrate upon neural tube defects, cardiac disease and more specific abnormalities, e.g. facial and limb deformities. Many abnormalities have now been demonstrated within the fetal abdomen and it is important to appreciate the significance of these abnormalities as there are, frequently, management implications. There are three major groups of fetal abdominal

abnormalities: (1) gastrointestinal, including obstruction, anterior abdominal wall defects, liver and biliary tree; (2) renal, including obstruction, cystic disease and renal agenesis; and (3) miscellaneous, including cystic intraperitoneal masses, cutaneous and subcutaneous lesions. Many of these abnormalities have important associations, e.g. a fetus with an exomphalos has a 30% incidence of a neural tube defect, 30% incidence of cardiac anomaly and 30% incidence of a chromosomal defect. The association with chromosomal defects is a repeated message when considering any fetal abdominal abnormalities. Examples include duodenal atresia and trisomy 21, anorectal atresia and trisomies 18 and 21,

polycystic kidneys and trisomy 13. The major conclusions in terms of possible management implications with *in utero* diagnosis of fetal abdominal abnormalities include the following. The ultrasonographer should be aware of the chromosomal associations and, if necessary, advise amniocentesis, both in early pregnancy with regard to possible termination and also in the third trimester to aid management decisions, *e.g.* caesarian section, at delivery. Some of the minor abnormalities, *e.g.* unilateral renal tract dilatation, should be monitored only during pregnancy and an early post-natal scan recommended. For severe abnormalities, *e.g.* gastroschisis, *in utero* transfer to a centre with appropriate neonatal medicine and surgical features should be considered.

Post-abortion fetal assessment using ultrasound and radiology

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The increasing routine use of ultrasound for estimation of gestation in obstetric units has dramatically increased the ante-natal diagnosis of fetal abnormality and led to a corresponding rise in therapeutic abortion. Diagnosis of neural tube, urogenital and abdominal wall abnormalities is well established and that of congenital heart defects has improved with the routine use of Doppler ultrasound in patients known to have had a previously affected child or fetus or those with a family history. Increasingly, however, these diagnoses are being made in patients without a family history and at an earlier stage of pregnancy. If we are to recommend termination in such cases it is vital that we avoid false positive diagnoses. The post-termination pathological examination plays an important role in this context. However, parents do not always accept the need for this. In addition, in some cases such as hydrocephalus, although the abnormality is clear it is difficult to be certain of the level of obstruction, if present, and thus to make a definitive diagnosis of the underlying cause. We present some recent cases in which post-termination ultrasound and other radiological investigations were used in addition to or occasionally in place of pathological examination to aid in diagnosis. Ultrasound has been of particular value in urological abnormalities. We feel that it is essential that careful pathological investigation with the use of imaging techniques where appropriate is performed routinely following therapeutic abortion in order that the maximum amount of information regarding the fetus is obtained. Only in these circumstances will it be possible to both monitor our own practice and provide appropriate counselling for the parents.

Fetal diaphragmatic hernia: the value of fetal echocardiography in predicting neonatal outcome

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Nineteen cases of congenital diaphragmatic hernia referred for fetal echocardiography during a 3-year period have been reviewed. In all cases the fetal heart was displaced from the normal thoracic position by the presence of the abdominal organs with the fetal chest. Congenital heart disease was diagnosed pre-natally in three cases; in one case associated with Trisomy 18 the pregnancy was terminated and the two

continuing pregnancies resulted in neonatal deaths. Qualitative and quantitative features of thoracic anatomy in the 16 cases of isolated congenital diaphragmatic hernia are correlated with post-natal outcome. Polyhydramnios and fetal hydrops were not associated with a poor post-natal outcome. The presence of the fetal stomach within the thorax was associated with the diagnosis of a large diaphragmatic defect, and a survival rate of 50%. A survival rate of 100% was associated with an abdominal site. Cardiac ventricular disproportion usually indicates severe fetal congenital heart disease. It may also be observed in the presence of an isolated congenital diaphragmatic hernia but in these circumstances the ventricular hypoplasia is reversible during infancy. Twelve of the 16 cases of isolated diaphragmatic defect were observed to have an RVID/LVID ratio outside the normal range during the ante-natal examination. Early evidence of ventricular disproportion indicated severe pulmonary hypoplasia and a poor post-natal outcome (100% mortality). Development of ventricular disproportion during the third trimester was associated with a survival rate of 75%. In three cases the cardiac appearance was normal during the third trimester examination (survival 100%). The detection of ventricular hypoplasia appears to be related to the degree of lung hypoplasia and therefore is associated with the requirement for prompt and prolonged aggressive ventilation from the time of delivery. The presence of ventricular disproportion during the second trimester in isolated diaphragmatic hernia is of potential value as a prognostic indicator.

The morbidity and mortality associated with an ante-natal diagnosis of bilateral fetal uropathy

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Pre-natal diagnosis of urinary tract anomalies has been established as being accurate and of value to post-natal management. The potential benefit is, however, offset when the abnormality is bilateral by the poor prognosis often associated with this finding. It had been hoped that intrauterine drainage of the urinary tract would help to reduce the morbidity and mortality associated with bilateral fetal uropathy, but at the present time there is no convincing evidence that this is the case. We have reviewed 54 cases of bilateral fetal uropathy detected between 1982 and 1987, to assess the incidence of coexistent pathology and the overall morbidity and mortality in these cases. Thirteen (24%) pregnancies were terminated. Of the 41 live births, 10 died, five from renal and/or pulmonary insufficiency and five in association with other congenital abnormalities. Thirty-one infants survived in whom a further four are known to have other significant pathology, and/or a poor prognosis for long-term survival. All 27 infants with isolated renal tract pathology received prompt treatment following delivery and all but two have excellent prospects for normal renal function. Bilateral fetal uropathy is associated with a high morbidity and mortality. In many cases, careful ante-natal assessment of the fetus by ultrasound, amniocentesis and analysis of fetal renal function will help to identify the fetus with a poor prognosis. Infants with isolated urinary tract pathology have a good prognosis if treated promptly following delivery. Our results compare favourably with published series following intrauterine intervention suggesting that the case for fetal surgery has not yet been clearly established.

Cardiac scanning at 13–15 weeks gestation

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In 8 years experience of fetal echocardiography, over 7000 pregnancies have been studied. It has been established that normal fetal cardiac anatomy can be defined from 18 weeks gestation onwards. In view of the proposal to change the abortion law in this country, we studied a number of pregnancies between 13–15 weeks gestation. The patients were picked at random from our routine clinic. The aim of this study was to establish the details of cardiac anatomy that can be

identified between 13–15 weeks gestation. The structures that were noted were the four cardiac chambers, the arterial connections, the insertion of the two atrioventricular valves, and the pulmonary veins. Apart from the pulmonary veins, all the other structures could be identified in all the cases studied. The pulmonary veins could be seen in 13 out of 20 patients. However, there are some types of congenital heart disease that cannot be accurately diagnosed at this early stage of gestation. One of the limiting factors in diagnosis is the quality of image obtained. This was found to be dependent on the fetal position, and maternal size.

Posters

- Aneurysm of the inferior pancreaticoduodenal artery diagnosed by real-time ultrasound and pulsed Doppler, by P. Grech, P. Rowlands and M. Crofton
- Ultrasound-guided biopsy of the transplanted kidney, by M. L. Nicholson, A. K. Attard, A. Bell, P. K. Donnelly, P. S. Veitch and P. R. F. Bell
- Ultrasound artefacts in hepatic steatosis, by C. E. Ingram, A. Moody, S. H. Saverymuttu and A. E. A. Joseph
- Caecal infarction mimicking carcinoma, by L. Yeoman, P. Mills and A. E. A. Joseph
- Female, fair, fat and forty = gallstones: true or myth?, by M. Gowland, S. Fielding, P. Crannage, G. Wright, B. Sherbourne and M. Nicol
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- Can ultrasound detect granulomatous liver disease?, by P. Mills, S. Saverymuttu, M. Fallowfield, S. Nussey and A. E. A. Joseph
- Doppler echocardiographic findings in a horse with mitral regurgitation, by C. M. Marr, D. Northridge, S. Love, J. Ndungu and J. S. Boyd
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Aneurysm of the inferior pancreaticoduodenal artery diagnosed by real-time ultrasound and pulsed Doppler

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Aneurysms of the superior mesenteric artery are rare, being noted in only one of 12 000 autopsies (Lucke & Rae, 1921). Aneurysms of branch arteries are even less common. Presentation is most commonly at the time of rupture, which often results in catastrophic and usually fatal haemorrhage. The

incidental finding of such aneurysms and their recognition thus assumes an importance out of proportion to their frequency. In the past, the diagnosis of visceral artery aneurysm has not initially been considered when a radiolucent mass was detected by ultrasound, resulting in delayed diagnosis or diagnostic puncture (Ugolotti et al, 1984; Mourad et al, 1987). Visible pulsation may be absent and an alternative diagnosis of pancreatic or mesenteric cyst considered. A case is presented in which an incidental finding of an asymptomatic aneurysm of the inferior pancreaticoduodenal artery was made by ultrasound

and pulsed Doppler; the diagnosis and exact anatomy were confirmed by angiography. A 50-year-old woman was referred for ultrasound examination of the pelvis for an unrelated problem. The patient was a normotensive non-smoker and on direct questioning revealed no symptoms referable to the gastrointestinal tract or upper abdomen. The ultrasound examination revealed a 23 mm diameter sonolucent mass in the upper abdomen immediately anterior to the aorta. The mass was pulsatile and appeared to lie postero-medial to the superior mesenteric artery but communicated with it. Pulsed Doppler revealed pulsatile but turbulent arterial flow within the mass and reliably excluded pancreatic mesenteric cyst. Angiography revealed a previously unsuspected stenosis of the proximal coeliac axis. The superior mesenteric artery was normal but there was aneurysmal dilatation of its first branch, the inferior pancreaticoduodenal artery, which provided a collateral blood supply to the post-stenotic coeliac axis. The aneurysm and stenosis were thought to be due to fibromuscular hyperplasia. More common causes of such aneurysms are arteriosclerotic disease and septic emboli.

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Ultrasound-guided biopsy of the transplanted kidney

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Renal transplant biopsy is an essential tool in the investigation of acute graft dysfunction. Percutaneous biopsy using the Trucut biopsy needle yields excellent histological material but is not without risk to both the graft and the patient. Prior to August 1986, transplant biopsies in this unit were performed using a "blind" vertical pass of the Trucut needle into one pole of the transplanted kidney. More recently, we have used a new technique incorporating real-time ultrasound scanning to guide the biopsy needle. The aim of the latter method is to allow more accurate positioning of the Trucut needle in order to biopsy selectively the cortex of the kidney and avoid the potentially dangerous medullary region. We have performed a retrospective study to compare the success and complication rates of the two methods. Two hundred and thirteen consecutive renal transplant biopsies were studied. All biopsies were obtained using a Trucut needle by either the vertical pass technique ($n = 69$) or the ultrasound-guided technique ($n = 144$). A total of 98 and 262 cores were obtained, respectively, and submitted for histological assessment. The results (see table) demonstrate that the ultrasound-guided technique was significantly more successful in achieving the aim of sampling the renal cortex alone.

	Renal cortex only in biopsy	
	+	-
Ultrasound guided	82.3%	17.7%
Vertical pass	62.6%	34.4%
$\chi^2 = 7.239$ (df = 1)		
$p = < 0.05$		

The mean glomerular count per biopsy was 15 in the ultrasound group and 5 in the vertical pass group ($p < 0.01$, Mann-Whitney *U*-test). Macroscopic haematuria occurred in 13 cases (9%) in the ultrasound group in five cases (7.2%) in the vertical pass group. Transfusion and exploration of the graft were required in one and two of these cases, respectively. These data demonstrate that ultrasound-guided biopsy yields a higher percentage of adequate biopsies than the vertical pass technique. The procedure has a low complication rate and we now employ it for all transplant biopsies.

Ultrasound artefacts in hepatic steatosis

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Several artefacts caused by hepatic steatosis have been described in the past in liver ultrasonography. We describe four new artefacts which may occur in the presence of hepatic steatosis. (1) *Hypoechoic pancreas*. A discrepancy between the level of echoes in a fatty liver and the adjacent kidney is well recognized. A similar discrepancy may be seen in relation to the pancreas, the latter appearing unusually echo-poor because of increased attenuation of the beam by the fatty liver, before it reaches the pancreas. (2) *Venetian blind sign*. A striped pattern within the fatty liver (a vertical "Venetian blind") is not uncommon. This is attributable to multiple small foci of fat causing more attenuation than the surrounds, giving a pattern of narrow echo-poor bands in an echogenic liver. This feature may also be seen with fibrosis. (3) *Stilette sign*. In cases of intrahepatic bile duct dilatation, the usual double channel appearance is modified by steatosis. The echogenic walls of the bile duct and portal vein that are adjacent to the liver merge with the high level of liver echoes, leaving the appearance of an echo-free tube containing a central echogenic line (composed of the adjacent portal vein and bile duct walls), which resembles a stilette or a needle within a sheath. Other echogenic walls may also be obliterated by the high level of liver echoes, in an ultrasound version of the silhouette sign; the gallbladder wall may also be lost in cases of severe fatty change. (4) *Pseudocystic lesions*. Solid lesions occasionally have a pseudocystic appearance. As in the case of liver/kidney discrepancy, the lesion appears echo-poor because fewer echoes penetrate through the highly attenuating fat. More echoes reach beyond the lesion than penetrate the fatty liver at the same level, leading to posterior enhancement. The resulting appearances, particularly the posterior echo enhancement, may lead to solid lesions being interpreted as being cystic.

Caecal infarction mimicking carcinoma

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A 50-year-old woman with unstable angina underwent cardiac catheterization. During the procedure, an abdominal aortic dissection occurred and the femoral catheter was withdrawn. The procedure was completed via the brachial route. Four hours later, she complained of abdominal pain localized to the right iliac fossa. An abdominal ultrasound examination performed after 24 h because of persistent pain confirmed a dissection of the abdominal aorta, which extended up to and beyond the origin of the superior mesenteric artery. Marked thickening of the wall of the terminal ileum, caecum and proximal ascending colon was noted, giving the impression of a mass. However, in view of the aortic dissection and history, a diagnosis of bowel infarction was made. The patient underwent laparotomy at which infarcted terminal ileum, caecum, and proximal ascending colon were removed. Histopathology confirmed the diagnosis. Bowel wall thickening can be recognized on ultrasound examination. The differential diagnosis to be considered includes carcinoma, lymphoma, infarction, and inflammatory causes such as Crohn's disease, tuberculosis, and amoebiasis. The wall thickening is usually less marked in infarction than in carcinoma, and this case is unusual in the degree of thickening shown. However, the involvement of the terminal ileum and extent of the abnormality on ultrasound together with the clinical history were highly suggestive of the diagnosis.

Female, fair, fat and forty = gallstones: true or myth?

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The classical symptoms of gallstones are right upper quadrant pain and tenderness and fatty intolerance, accompanied with a history of nausea and vomiting. Routine ultrasound of the gallbladder can reveal incidental and completely asymptomatic gallstones or negative findings in patients with typical symptoms of gallbladder disease. In view of these discrepancies between sonographic findings and patients' clinical diagnostic history, a study was undertaken to identify a correlation between symptoms and the presence of gallstones. One hundred patients referred for ultrasonography of the gallbladder were asked a series of questions regarding their age, height and weight and females were asked the number of confinements, the type, site and duration of pain and its relationship to specific foods, if any, and additionally if nausea or vomiting was present. The scans were performed using a Diasonics DSI RF real-time ultrasound machine with a 3.5 MHz mechanical sector probe; hard copy was recorded using a multifformat matrix imager. A table of the results of our study is presented together with images and illustrations of our findings in these patients.

What's new in ultrasonography of portal hypertension?

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Stomach and gallbladder wall thickness of 27 patients with histologically proven cirrhosis and endoscopically demonstrable varices were compared with 21 control patients.

Measurements were made in the antrum and the body of the stomach in the supine position after an overnight fast. Gallbladder wall measurements were also made. Serum albumin levels were measured within 48 h of the ultrasound examination. Results of measurements made of the stomach are given below.

	Control	Cirrhotic
Antrum	Mean 13.8 mm, SD 3.02 Range 8–20 mm	Mean 22.15 mm, SD 5.63 Range 13–31 mm
Body	Mean 14.05 mm, SD 2.70 Range 11–19 mm	Mean 22.2 mm, SD 5.73 Range 13–31 mm

($p < 0.01$)

Can ultrasound detect granulomatous liver disease?

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The use of ultrasound to both diagnose and monitor hepatic parenchymal disease is becoming more widely accepted. The characteristic features of fat and fibrosis in the liver are now well recognized. We have noted an abnormal echo pattern in patients with granulomatous liver disease and have therefore reviewed the ultrasound scans of 11 patients with biopsy proven granulomatous liver disease. The final diagnoses were sarcoidosis in five patients, miliary tuberculosis in three, brucellosis in one and in two patients the aetiology is unknown. At the time of scanning, the liver was noted to be abnormal in all cases and in seven cases a specific diagnosis of granulomatous liver disease was suggested. All patients underwent liver biopsy within 1 week of the scan, except one. Two patterns of abnormality were recognized. All patients had small (3–6 mm) moderately echogenic lesions with an echo-poor halo. Three patients had similar lesions in the spleen. Two patients also had multiple hypoechoic lesions (2–3 mm) arranged in clusters. One of these patients had miliary tuberculosis and the aetiology is unknown in the other. To our knowledge, lesions of this type have not been previously described in association with granulomatous liver disease. It should be noted that *Streptococcus milleri* abscesses, lymphoma and small metastases may mimic granulomas in the liver. Miliary abscesses are usually hypoechoic, often larger than granulomata and irregular in shape. In summary, we believe that granulomata can be demonstrated in the liver using ultrasound. If either of the described appearances are seen on a liver ultrasound examination, a diagnosis of granulomatous liver disease should be considered.

Doppler echocardiographic findings in a horse with mitral regurgitation

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A 6-year-old Irish Draft cross gelding was presented to Glasgow University Veterinary School with sudden onset

dyspnoea following light exercise, a serosanguinous nasal discharge and elevated pulse and respiratory rates. On auscultation, a Grade IV/V holosystolic, regurgitant murmur was detected with its point of maximum intensity over the mitral area. It radiated widely, in caudal and dorsal directions, and a loud ventricular filling sound was also present. The inspiratory and expiratory sounds were harsh across the entire lung field. Phonocardiographic examination confirmed these findings. The electrocardiographic features were within the normal equine range and haematological examination indicated leukocytosis and neutrophilia. M- and B-mode echocardiographic examination demonstrated left arterial enlargement with dilatation of the left ventricle. A regurgitant jet was identified in the left atria using pulsed and continuous-wave Doppler echocardiography, which confirmed the presence of mitral regurgitation. Mitral regurgitation is an uncommon but serious condition in the horse and it has been reported in association with signs of left cardiac failure and in horses demonstrating no clinical signs at rest, with mild exercise tolerance. The prognosis for the condition is poor. Incompetence of the left atrio-ventricular valve exposes the pulmonary vasculature in high systolic pressure leading to pulmonary oedema. In the past, this diagnosis in the equine has been based on findings of clinical, phonocardiographic examinations and cardiac catheterization. This case demonstrates the successful confirmation of mitral regurgitation by non-invasive means using Doppler echocardiography.

Acknowledgments

The ultrasonographic unit used in this case was purchased with an award from The Home of Rest for Horses.

Congenital cardiac disease in domestic animals: comparison of echocardiographic and pathological findings

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The echocardiographic findings in various congenital cardiac conditions were compared with the pathological features. In ventricular septal defect, a lesion was identified in both long- and short-axis images of the left heart and it was located at the base of the aorta. Tetralogy of Fallot in the calf resulted in a large ventricular septal defect at the aortic root, right ventricular hypertrophy and dilatation, over-riding aorta and pulmonic stenosis. Microbubble contrast medium inserted in the jugular vein appeared in the left ventricle and demonstrated the presence of a right to left shunt. Bovine aortic dysplasia produced left ventricular and aortic dilatation and on longitudinal and transverse images of the aortic valve, two shrunken and thickened cusps were identified with the configuration of the third being normal. Atrial septal defect was diagnosed in a dog in which there was enlargement of both atria and hypertrophy of the right ventricle. Microbubble contrast medium administration was required to demonstrate the defect. In all cases these findings were confirmed on post-mortem examination. Two-dimensional echocardiography is becoming increasingly widely used in veterinary medicine in the diagnosis of both congenital and acquired cardiac lesions. In these examples it allowed visualization of the cardiac chambers, valves and great vessels and their anatomy was defined. The haemodynamic effects of cardiac lesions could be documented

and their presence supported the diagnosis. The use of the microbubble contrast medium technique was advantageous in those conditions associated with right to left shunts.

Acknowledgments

One of the ultrasonographic units used in this study was purchased with an award from The Home of Rest for Horses.

Sonographic measurement of renal length and renal volume in the dog

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The right and left kidneys of 100 mature dogs were examined. About half of these dogs were shown to have normal kidneys on intravenous urography. A catheterized urine sample was negative on bacterial culture in each case. The remaining dogs were subsequently shown to have normal kidneys at post-mortem examination. Two standard planes of section were imaged in each kidney and measurements of renal width, length and depth were obtained. Estimates of renal volume were calculated using the formula for the volume of an ellipsoid. A strong positive correlation was found between renal length and body weight, and between renal volume and body weight.

The influence of the measurement site on umbilical artery flow velocity waveforms

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Umbilical artery flow velocity waveforms (FVW) have been widely investigated as a possible indicator of fetal compromise due to placental insufficiency. Many authors have identified and confirmed the changes in FVW associated with increasing gestational age and the decrease or loss of diastolic flow in cases of impaired fetal growth. Most studies so far have employed continuous-wave Doppler signals from the umbilical artery without the advantage of simultaneous B-mode imaging to identify a similar site along the cord for each patient. We have recorded the FVW at three sites along the umbilical artery in 24 normal pregnancies to see if there is any significant difference in waveform indices between sites. The umbilical artery was located using the 3.5 MHz sector transducer of an Acuson 128. The three sites chosen for pulsed Doppler evaluation were: (a) within 2 cm of placental cord insertion, (b) within 2 cm of fetal cord insertion and (c) mid-cord. Having identified each site, pulsed Doppler mode was entered with simultaneous two-dimensional imaging being maintained until an adequate Doppler spectral display was achieved. At least 10 waveforms from each site were recorded for later analysis and calculation of waveform indices. A summary of our results is presented.

Amniotic fluid volume

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Amniotic fluid volume plays an important role in normal fetal growth and development but its accurate measurement has proved difficult. The methods in use include: (1) total

intrauterine volume measurement, which is impractical in many cases, (2) subjective assessment of fluid volume, which is prone to observer variation and (3) measurement of the deepest vertical pocket of fluid. There is little published information available on pocket size throughout pregnancy. The purpose of this report is to provide data from 16 to 42 weeks gestation obtained by measuring the maximum depth of the deepest pool. In the 3-year period from 1985 to 1987, the records of all scans carried out in the Queen Mother's Hospital were filed in the Glasgow University mainframe computer. All singleton pregnancies in whom ultrasound dating had been performed before 20 weeks were selected for analysis. Amniotic fluid volume was recorded as the maximum vertical depth of the deepest pool of fluid. All amniotic fluid measurements recorded were included. There is no routine later scanning policy at the Queen Mother's Hospital and all scans were clinically indicated for various reasons. The centile values calculated from the raw data are as follows.

Gestation (weeks)	No. of measurements	5	10	50	90	95
16	22	35	38	54	76	87
17	33	33	37	47	71	80
18	38	38	40	55	88	96
19	28	30	39	50	71	72
20	26	37	42	56	64	68
21	21	45	45	55	76	78
22	19	10	40	54	78	83
23	32	41	49	62	77	88
24	42	45	48	66	79	85
25	53	41	47	70	98	100
26	79	39	45	69	90	98
27	80	38	45	65	90	93
28	117	35	42	62	85	94
29	121	36	43	66	93	110
30	175	40	48	65	82	91
31	174	43	49	66	90	96
32	202	42	45	61	88	96
33	234	40	47	61	81	91
34	313	40	45	62	82	91
35	277	40	45	65	88	100
36	410	39	44	60	81	91
37	402	40	43	60	83	90
38	335	35	40	59	82	93
39	263	35	40	58	82	94
40	172	32	37	58	78	85
41	278	30	35	59	79	87
42	42	24	30	52	74	78

The accuracy of ultrasound localization of the anatomical site of neural tube defects

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Neural tube defects (NTDs) are the most common cause of fetal anomaly in the United Kingdom. With the advent of maternal serum α fetoprotein screening, amniocentesis and high-resolution ultrasound equipment, the vast majority of these defects are amenable to accurate diagnosis. Since 1983 we have diagnosed 59 cases of NTDs in our unit: 23 cases of anencephaly, 27 cases of spina bifida cystica, four

encephalocoeles and five miscellaneous cranial anomalies. We are currently comparing the accuracy of pre-natal ultrasound diagnosis with post-delivery radiological and post-mortem examination with regard to the accuracy of localization and delineation of the lesion. The diminishing role of amniocentesis in the management of these cases is discussed.

Short-term variability of the Doppler flow velocity waveform in several sites of the umbilical artery and the fetal aorta

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Several authors have reported the reproducibility of Doppler flow velocity waveform (FVW) measurements in the umbilical artery waveform using continuous-wave (CW) systems. Even with the synchronous use of real-time imaging, it is not possible to select confidently a particular portion of the umbilical cord for study. We elected to study whether there were any significant changes in the FVW measurements in three separate regions of the cord and two sites of the fetal aorta. Satisfactory recordings from 20 patients have been studied to date. All of the pregnancies were uncomplicated and between 36–40 weeks gestation. Oral informed consent was obtained from each patient. All of the examinations were performed using a pulsed Doppler system with a 4-s real-time image update (Diasonics 300CV, 3.5 MHz probe, 100 MHz thump filter). The range gate was applied over the selected vessel and narrowed appropriately prior to recording. The procedure was abandoned if fetal breathing was apparent. The cord insertions into the fetus and placenta and a mid-loop of cord were sampled as were the thoracic and abdominal portions of the fetal aorta. Flow velocity waveform traces were recorded onto high-quality metal tape and analysed by a DOPTEK spectrum analyser. Traces complicated with fetal breathing were excluded from further analysis. The A/B ratio, RI and pulsatility index were measured. We have failed to show any significant difference in any of the parameters measured related to changing the portion of the vessel studied. The short-term variability was of the order of 5–10%, which is in keeping with other workers' findings.

The significance of absent end-diastolic flow in the umbilical artery

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Absent end-diastolic flow (EDF) in the Doppler flow velocity waveform (FVW) of the descending fetal aorta has been associated with intrauterine fetal hypoxia and significant neonatal complications. We have studied the relationship between absent umbilical artery, EDF and pregnancy outcome. Twenty-three high-risk pregnancies were studied. Sixteen were complicated by moderate/severe pregnancy-induced hypertension (PIH) defined by a diastolic BP persistently > 100 mmHg and seven were complicated by a small-for-dates (SFD) fetus without maternal hypertension. All of the PIH group were treated with antihypertensive drugs (Labetalol $\pm$ Nifedipine). Umbilical artery FVWs were recorded with a DOPTEK continuous-wave system (4 MHz probe, 150 MHz thump filter). Waveform patterns were defined by the pulsatility index (PI). The clinicians responsible for patient management were blinded to the Doppler results. The interval

between the last Doppler recording and delivery was less than 7 days. Absent EDF was detected between 0 and 18 days prior to delivery in seven pregnancies with SFD infants (mean gestational age 33.7 weeks, range 31–36). Intrauterine death occurred in one case and one infant has congenital malformations. The remaining five infants are thriving. Sixteen pregnancies complicated by moderate/severe PIH were delivered at a mean gestational age of 31 weeks (range 26–36 weeks). Absent EDF was detected between 0 and 35 days prior to delivery. Intrauterine death occurred in six cases, NND in one case and of the nine survivors, one infant has severe disabilities. It is apparent that absence of EDF in the umbilical artery does not in itself indicate an adverse pregnancy outcome. It is important to note that gestational age significantly influences outcome. Using death as the end-point, the outcome in the PIH group <31 weeks was significantly worse compared with the >31 week PIH group ($p = 0.003$, Fisher's test).

The outpatient management of potential incomplete abortion using ultrasound imaging and oral ergometrine therapy

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One hundred consecutive patients with a diagnosis of incomplete abortion underwent ultrasound imaging of the uterus at presentation. The patients were in the first trimester and were not suffering from severe haemorrhage or infection. Retained products of conception were diagnosed if the central uterine echo was more than 5 mm deep and not homogeneous. Twenty-six patients were found to have a normal uterine cavity and were discharged. The remaining 74 patients were given a course of oral ergometrine for 2 to 3 days as outpatients. Following the course of ergometrine, the patients were re-examined with ultrasound. Forty-eight were found to have a normal uterus and were discharged. Only 26 patients (36% of those with retained products) required evacuation of the uterus under anaesthesia. One patient re-presented after 6 weeks with recurrent bleeding, having been discharged following ergometrine therapy and a normal ultrasound examination; she was subsequently evacuated. The management of incomplete abortion with ergometrine therapy and ultrasound imaging can substantially reduce the number of patients who require evacuation of the uterus.

How accurate are ultrasound measurements in the non-pregnant pelvis?

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A study was conducted to compare the measurements of the uterus and ovaries recorded by ultrasound with the measurements taken during hysterectomy. The aim of the study was to show how accurate the ultrasound measurements were. Thirty-eight women were studied. Ultrasound was performed by one of two observers on the day preceding surgery for hysterectomy $\pm$ oophorectomy. The uterine length, uterine depth, the endometrium and the ovarian dimensions in three planes were collected. The presence and dimensions of follicles were also recorded. The following day during surgery the

uterus was remeasured shortly after being removed and prior to immersion in formal saline. The ovaries were measured either after oophorectomy or during the procedure if they were being conserved. The uterus (and ovaries) were again measured in the laboratory after being immersed in formal saline. Significant correlation was found when comparing uterine dimensions. Correlation coefficients of 0.94 and 0.83 were recorded for uterine cross-sectional area and endometrial thickness. Analysis of the comparative values for ovarian volume revealed correlation coefficients of 0.78 and 0.84 for the right and left ovaries, respectively. The use of ultrasound as a diagnostic tool in gynaecological practice is widespread. The present study illustrates a good correlation between ultrasound observations and the findings at laparotomy.

The choice of index for umbilical artery Doppler waveforms

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There have been a large number of studies over the last few years that have assessed the use of Doppler ultrasound of the umbilical artery. A number of parameters have been used to characterize the degree of diastolic flow, including resistance index (RI), pulsatility index (PI) and A/B ratio. This study investigates the power of a number of waveform indices in the prediction of antenatal fetal compromise. Two hundred and eleven patients were studied. This included 111 patients with growth retardation but no other pregnancy complication or pre-existing maternal disease, 94 with hypertension and six with ante-partum haemorrhage. Thirty-eight patients had ante-natal fetal compromise. Doppler waveforms were acquired from the umbilical artery using a 4 MHz CW device (Doptek) and stored on audiocassette for later analysis. Doppler waveforms were analysed using a BBC microcomputer. A number of indices were calculated including resistance index (RI), pulsatility index (PI), downslope (DS), and half peak time ("resistance time" (RT)); ROC curves were drawn. Statistical analysis using McNemars test at a fixed sensitivity of 100% showed that there was nothing to choose between PI and RI, but DS and RT were significantly worse. It is concluded that as RI does not require software calculation, it is the index of choice for prediction of ante-natal fetal compromise.

The effect of maternal exercise on fetal umbilical waveforms

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Twenty-one nulliparous women in the last trimester of pregnancy gave their informed verbal consent to undergo an acute non-weight-bearing exercise test for 5 min on a bicycle ergometer. Fetal umbilical artery velocimetry waveforms were measured using a linear array scanner and pulsed Doppler ultrasound. The mean gestation was 32 weeks (range 28 to 37 weeks). The mean exercise intensity was 71% of submaximal exercise (range 67 to 74%) and maternal heart rate rose significantly ($p < 0.001$) from a mean of 83 to 138 beats per minute. Fetal umbilical artery velocimetry waveforms were measured before and after exercise. The placental resistance index was used by estimating the peak systolic over the end diastolic value, the S/D ratio. Following moderate exercise, the

S/D ratio decreased significantly ($p < 0.001$) after 2 and 20 min. It is concluded that maternal exercise causes a decrease in placental vascular resistance and therefore may cause an improvement in placental circulation following exercise in healthy individuals, which is not hazardous to the fetus at this level of exercise. *Note.* This is the pilot study and the analyses on the umbilical and the uterine arteries blood flow of 120 cases are available.

Doppler ultrasound of the utero-placental circulation as a screening test for hypertension and intrauterine growth retardation

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One thousand and four primae parae underwent continuous-wave Doppler investigation of the utero-placental circulation at 18–20 weeks gestation as a possible screening test for hypertension in pregnancy. With the woman in a semirecumbent position, a continuous-wave Doppler ultrasound medicine with a 4 MHz transducer was used to obtain signals from utero-placental vessels on either side of the uterus. Women with abnormal waveforms ($RI > 0.58$) suggestive of high utero-placental resistance were tested again at 24 weeks when 105 demonstrated a persistent abnormality. After delivery notes were examined for evidence of hypertension, proteinuria and intrauterine growth retardation, sensitivity, specificity and predictive values were calculated. The efficiency of the test as a predictor of mild-to-moderate hypertension was compared with its ability to predict severe complicated pre-eclampsia. The prevalence of hypertension during the study period was 6.9% whilst that of proteinuric hypertension was 2.0%. Continuous-wave Doppler ultrasound identified, at 24 weeks' gestation, 68% of patients who developed proteinuric hypertension and 94% of patients whose hypertension was complicated by intrauterine growth retardation. Doppler investigation of the utero-placental circulation at 24 weeks is a sensitive, simple, non-invasive screening test for severe pre-eclampsia. On the basis of these results a randomized, double-blind, controlled trial of low-dose aspirin has been commenced.

Is Doppler ultrasound beneficial in obstetric management?

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There has been much debate on the clinical role that fetal blood flow assessment using Doppler has to offer. We studied 50 pregnancies in which the mother was clinically suspected of having a pregnancy complicated by intrauterine growth retardation (IUGR) and subsequently delivered in an infant with a birth weight below the 10th or 3rd centile for gestational age. For all patients the gestational age was confirmed by ultrasonographic measurement at the BPD at 16–18 weeks. Doppler blood flow studies of the fetal and utero-placental circulations were performed within 3 weeks of delivery using either a 4 MHz continuous-wave Doppler transducer or an ultrasonic duplex system. For the utero-placental circulation the flow velocity waveforms (FVW) were recorded from the uterine wall bilaterally. The waveforms representing the lowest

vascular resistance were used to calculate the pulsatility index (PI). At least 10 consecutive cycles were used for calculation of PI from the umbilical artery FVW and at least six consecutive cycles for utero-placental circulation. The eventual outcome of the pregnancy was related to the ante-natal Doppler findings. Our normal range of waveform indices was derived from studies on 333 pregnancies with a normal outcome. There was a strong relationship between those infants recognized as suffering complications of IUGR (necrotizing enterocolitis, hypoglycaemia, perinatal death, etc.) and abnormal FVW in umbilical and utero-placental circulations. However, all those pregnancies complicated by abnormal FVW were identified clinically and ultrasonographically as having severe IUGR. The significance of these findings is discussed in the context of employment of Doppler investigations in routine clinical practice.

Quantitative mapping of acoustic and histological properties of excised tissues

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This poster describes apparatus and techniques developed to improve our understanding of the physical basis for the diagnostic use of existing ultrasound methods, and of the potential value of quantitative approaches to tissue characterization; of particular interest are homogeneous tissue regions, such as liver metastases or breast carcinoma. Each freshly excised specimen is degassed, embedded in gelatin and examined with a real-time B-scanner to select a section at which the image is digitized and a 7 mm thick slice is cut. This slice is then further divided to isolate a 3 cm by 3 cm region of interest. Automatic measurements are then made, at 1024 positions over the specimen and at up to 30 frequencies in the range from 3 to 7 MHz, of sound speed, ultrasonic attenuation coefficient, and the absolute backscattering coefficient. Each of the acoustic properties is displayed as an image, to observe their interdependence and to study their correlation with the spatial fluctuations of the histological characteristics of the tissues. After completing the acoustic measurements, the tissue slice is frozen and finely sectioned. These sections are stained for fat and collagen, and placed on the stage of a specially modified microscope. Under computer control the sections are scanned and, using digital colour subtraction, a quantitative picture of the spatial distribution of the percentage content of the stained component is built up. Multivariate statistical methods may be applied to the acoustical data to produce tissue correlation with histology and pathology. Having classified tissue regions it is then possible to identify regions of the original data from which to obtain good averages of basic acoustical quantities such as the frequency dependence of scattering, which are likely to provide information about the microscopic distribution of histological components rather than their total content.

The application of commercial test instruments to commissioning ultrasound imaging equipment

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The setting up of the Ultrasonic Equipment Evaluation Project (UEEP) in 1985 using the Cardiff Test System and other test equipment has enabled an improved quality assurance service

to be provided at District level. These reports list standard performance tests and results for a range of equipment. A selection of these tests is easily performed at District Hospitals and these have been found very valuable in commissioning new ultrasound imaging equipment. Six pieces of equipment have been commissioned in Leicestershire since the availability of these reports and our experiences are described.

In Leicestershire District, quality assurance is now mainly based on the following test equipment. (1) Cardiff resolution test object, (2) Cardiff grey-scale test object, (3) acoustic signal injection system tester, (4) digital video pattern generator AM1103, and (5) Leicester caliper test object. Item (5) is not available commercially and is used for sector scanners. The parameters examined are: (a) high-contrast penetration, (b) low-contrast penetration, (c) axial resolution, (d) lateral resolution, (e) uniformity, (f) dynamic range, (g) caliper accuracy, (h) geometric accuracy, (i) visual appearance of image, (j) performance of image recording system, and (k) clinical performance. Several faults were found in six items commissioned. Caliper errors of 5% were found on a phased array and 2% on a linear array. In two cases the grey-scale characteristic required re-adjustment for satisfactory clinical performance despite satisfactory dynamic range performance. General conclusions were as follows. (1) No order should be placed before an adequate technical specification has been provided. (2) All equipment should be carefully tested on delivery. (3) Useful improvements could be made in the following areas: (a) the provision of reproducible test images for all imaging equipment in the service of operating manuals, (b) a grey-scale tester for low-contrast performance, (c) an improved commercial caliper test object for sector scanners, and (d) better test object manuals.

Colour-coded Doppler flow imaging in peripheral vascular disease

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Duplex ultrasound systems combine Doppler blood flow spectra with real-time imaging. For the non-expert, spectral information can be difficult to interpret, and examination of the lower limb arterial system is time-consuming, since the sample volume must be positioned in multiple sites along the vessel. Colour-coded Doppler flow imaging allows real-time visualization of blood velocities superimposed in colour on the grey-scale image. This technique has been used successfully in cardiac ultrasound and we have investigated its application in the peripheral circulation. During a 6-month period, patients routinely referred to the Bioengineering Unit for investigation of lower limb arterial disease were studied using the Toshiba SS65A colour-coded system, employing a 5 MHz phased array transducer with water bath standoff. We found that colour coding allows a more rapid localization of disease. Turbulence and blood flow disturbances are readily identified and any suspicious areas may be interrogated further with conventional Doppler. In addition, the colour-coded presentation of the data is readily appreciated by clinicians.

Echocardiographic imaging of the aortic arch in adults

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Suprasternal notch is one of the "standard" recording positions used in echocardiography. From it, it is possible to image the

aorta (particularly the arch) and the pulmonary trunk. The suprasternal approach is employed frequently in children, but rarely in adults, and publications concerning adults have been confined to the investigation of coarctation of the aorta. The aims of our study were first to determine how often it is possible to image the aortic arch and its branches in adult subjects, and secondly to determine whether abnormalities of the branches (particularly athero-sclerotic occlusion) can be delineated. First, using the suprasternal approach, we attempted to image the aortic arch and its branches in 50 consecutive adults referred for echocardiography; satisfactory views were obtained in 30. Second, over the past 18 months, we included the suprasternal view in our examination of patients who were referred with symptoms of cerebrovascular disease and in whom extracranial vessel involvement was suspected. We obtained technically satisfactory images in 41 out of 55 studies and in a few patients we identified features consistent with atheromatous narrowing. Third, we have recently examined six patients who have undergone arch aortography in the past year; the echocardiographic findings correlated completely in all. We conclude that satisfactory ultrasound imaging of the aortic arch and its branches is feasible in the majority of adults, that the method has diagnostic potential and that this merits further evaluation.

Doppler echocardiographic measurement of cardiac output in patients with acute myocardial infarction

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Several non-invasive techniques have been used in the past to measure cardiac output (CO) but none has gained wide acceptance. Invasive determination using a Swan Ganz catheter remains the gold standard. Recently, remarkably accurate results have been claimed for Doppler echocardiographic (Dopp) measurements of CO. We have investigated the use of Dopp to measure CO. Firstly reproducibility was determined in six stable patients recovering from myocardial infarction (MI). Overall, Dopp measurements were highly reproducible with a coefficient of variation of 4.2%. We then compared Dopp with invasive measurements. Seventeen patients were studied within 24 h of MI. A total of 25 simultaneous comparisons were made between the results of Dopp and thermodilution. There was good agreement between the two techniques, with a correlation coefficient of 0.79. Furthermore, Dopp measurement of stroke distance correlated closely with stroke volume index determined by thermodilution ($r = 0.76$). Cardiac output determination by Dopp was reproducible and fairly accurate when compared with thermodilution of patients with acute MI. Furthermore, a good approximation to stroke volume index could be made from Dopp measurement of stroke distance alone.

Ultrasonographic test for fallopian tubes patency

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The patency of the Fallopian tubes is an essential investigation of women with infertility. Currently the two most widely applied tests for this investigation are hysterosalpingography and laparoscopic chromotubation (dye test). A new test utilizing an ultrasonographic technique for testing the patency

of the uterine tubes is described. The main advantages as well as the provisional results of this test are outlined.

Transvaginal ultrasonography and the IUCD

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Transvaginal ultrasonography is performed with a transducer of higher frequency than that used abdominally. This, in conjunction with the proximity of the probe to the pelvic organs, gives excellent image quality, even in the obese patient. The technique is now firmly established in infertility work and is becoming more widely employed in general gynaecology. We have assessed its potential for use in the management of women who have had an IUCD inserted. Ultrasonography was performed on 40 women attending the Family Planning Clinic of the Royal Maternity Hospital, Belfast. In 20 women the IUCD had just been inserted. The remaining 20 had returned to the clinic either to have the position of the IUCD routinely checked, because the strings could not be detected by the patient, or because of menstrual disturbance including suspected pregnancy. An Aloka 5 MHz mechanical sector transducer (Model UST-945P-945P-S) was used. The procedure was performed with the patient in the supine position and with the urinary bladder empty. The investigation proved acceptable to all women. It was described as being less uncomfortable than having a cervical smear taken and several women were reassured to actually see the IUCD *in situ*. The fact that the procedure is performed with the bladder empty increases its acceptability to patients and allows it to be performed without delay after insertion of the device. With this technique the IUCD is clearly visible in the uterine cavity ensuring correct insertion. It would be quite feasible to measure cavity length prior to insertion with this method. Confirmation of the correct position of the IUCD following insertion by a trainee would be advantageous and from a medico-legal viewpoint the fact that perforation of the uterus has not occurred at the time of insertion may be documented. The basics of this technique are readily learned and with further experience unsuspected pelvic pathology may be detected. Intrauterine pregnancies may be identified and extrauterine pregnancies may be suspected and confirmed at an early stage. From our experience we conclude that transvaginal ultrasonography will have a significant place in the management of women using the IUCD.

Transrectal ultrasound-guided transperineal fine-needle aspiration of the parametrium

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Cervical cancer spreads early to the soft tissue surrounding the cervix, which carries lymphatic and blood vessels. Determination of the invasion of this space is crucial in determining treatment and outcome. The traditional pelvic examination under anaesthesia is inaccurate in determining parametrial status. Several groups now attest to the use of transrectal endosonography in visualization of the parametrium, but even when suspicious appearances are obtained, distinction still needs to be made between benign inflammatory reaction and malignant infiltration. Fine-needle aspiration offers cytological corroboration. Its use in recurrent

tumour is well described. The patient, who has micturated 1–2 h previously, is placed in the left lateral position. After transvaginal sector scanning with a Bruel and Kjaer 7 MHz 8537 probe to determine uterocervical anatomy a 5.5 MHz 1850 radial probe is passed transrectally. Under aseptic conditions and with the intravenous injection of cefuroxime and metronidazole antibiotics, transperineal fine-needle aspiration is performed. The needle guide is attached to the probe and the grid software utilized. A 21-gauge needle and stylette are inserted into the suspicious area. Care is taken to avoid uterine vessels. The stylette is withdrawn, manual syringe aspiration is performed and the needle withdrawn. Scanning is resumed to observe any haematoma formation. If a satisfactory sample is obtained, this procedure is performed once only. The sample is smeared and fixed and sent for cytological examination. No complication has so far been observed. The procedure has so far been performed in six cases. Five have proven negative, three with radical hysterectomy corroboration. One has proven parametrial infiltration. The frequency of false negative results will be determined by long-term study.

Ultrasound evaluation of the "solitary" thyroid nodule

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Evaluation of a palpable solitary lesion is the commonest indication for ultrasound examination of the thyroid gland. The ultrasound features encountered in 1010 such patients have been analysed and correlated with the final pathological diagnosis, provided by histology or cytology in 317, with the following results. Additional thyroid nodules were identified in 23%. Amongst those surgically resected, the malignancy rate was 2.2%. Amongst solitary lesions, 20% were completely fluid filled without any mural solid elements, representing areas of haemorrhage within the gland. Such lesions had negligible risk of malignancy. The presence of an ultrasonic "halo" reduced the chance of malignancy, but only from 10 to 7%. If completely solid the risk of malignancy was 10.5%. The presence of a part-fluid component reduces this risk to 5.5%. "Dark" lesions are more likely to be malignant (14.6%) than isoechoic (7%) or "bright" lesions (8%). No focal nodule could be identified within the thyroid itself in six patients (2%). In 83% of these cases, the ultrasound diagnosis (metastatic carcinoma, Hashimoto's thyroiditis) was subsequently confirmed. Thus a solitary lesion which has any solid elements must be suspect of malignancy, regardless of its other sonographic features. However, since 90% of such lesions are benign, a diagnostic pathway based on an initial ultrasound examination, with selective use of fine-needle aspiration for cytology, is suggested.

Initial experience with the Berger neuro-biopsy device

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During this year, experience has been gained at The London Hospital in the use of the Berger neuro-biopsy device in association with a Diasonics DRF 100 ultrasound machine. The

technique for obtaining ultrasound images of the brain, and subsequent biopsy material, via a burr hole in the skull, is described and illustrated by pre-operative photographs. The device consists of a base plate, clamp plate, needle guide, probe swivel socket and locking ring. Two probes, a 5 MHz and 7.5 MHz, are employed depending on the depth of the lesion. Following delineation of the abnormality, the precise alignment of the probe is maintained by tightening of the locking ring and a biopsy needle inserted through the device to the appropriate depth. An advantage of the method is that it allows precise biopsy from the edge of the lesion where growing cells are likely to be found, as well as from any depth within it. Following biopsy the area can be re-scanned to ensure that no haematoma has resulted. So far 20 patients have been examined and satisfactory biopsy material obtained in each case. The lesions included tumours and abscesses and the technique applied to the posterior fossa as well as to supratentorial lesions. This initial experience suggests that the technique is superior to craniotomy with blind biopsy, where satisfactory material is often not obtained, and to CT-guided biopsy, which, although highly accurate, is cumbersome and slow. The method is also of value in aiding the placement of ventricular catheters.

Bubble recycling as the mechanism responsible for cavitation enhancement in a rotating tube

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The cavitation-promotion effect of rotating a sample tube during ultrasound exposure is not yet fully understood. Cavitation-induced haemolysis was observed in 0.5% haematocrit suspensions of erythrocytes exposed for 5 min at 37°C. For 1.61 MHz unfocused exposure with 6 dB beam width of 14 mm, an apparent threshold of 2–4 W/cm² spatial peak intensity was obtained for haemolysis in a 1.6 cm diameter exposure chamber, which was made of dialysis tubing and rotated at 72 rpm. If the tube was not rotated, then no haemolysis was observed up to 16 W/cm². Creation of standing waves in the sample by using a thick-walled culture tube or by placing a styrofoam reflector behind the dialysis tube did not change the apparent threshold. Focused 1.45 MHz exposure gave the same apparent threshold in the rotating dialysis tube, which was shortened to 8 mm for the 6 dB beam width of 2.6 mm. The apparent threshold increased to 128–256 W/cm² for the non-rotating case. When the focused ultrasound was turned on for half a rotation and off for half, results were similar to those for a non-rotating CW case, while on-off cycles synchronized to a quarter rotation gave results similar to the rotating CW case. These results lead us to suggest that cyclic nucleation at the tube wall could be important in cavitation promotion. Rotation brings bubbles on the rear wall, where the beam exits the tube, back around to the front again, where the

bubbles may then re-nucleate the suspension, and thereby promote cavitation bioeffects in the rotating tube.

A comparison of behaviour in the healthy term human fetus and newborn

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Behavioural studies have established that in the last few weeks of gestation, the human fetus develops behavioural states that appear similar to those of the newborn. These have been designated 1F, 2F, 3F and 4F to distinguish them from states S1 to S5 of the newborn (Nijhuis et al, 1982). Using real-time ultrasound, we have studied behaviour in 50 normally grown, low-risk singleton fetuses between 37 and 42 weeks gestation to determine the proportion of time spent in each behavioural state. Fifteen of the subjects underwent further evaluation of the same behavioural parameters between 3 and 5 days of age, in order to validate analogy between the fetal and neonatal behavioural states. We found that 2F was the predominant behavioural state (occurred in 49 fetuses, represented 57.4% of total recordings), and during most of the studies this cycled with 1F (occurred in 49 fetuses, represented 28.5% of total recordings). Fourteen of the fetuses exhibited state 4F (11.0% of total recordings), and in one case this persisted for the entire duration of the study (137 min). The maximum durations of 1F and 2F were 38 and 94 min, respectively. During only 3.1% of the study time were the behavioural parameters indeterminate. In the newborn studies we found that the eye movements, level of activity and heart rate pattern in S1 (quiet sleep), S2 (REM sleep) and S4 (active awake) were analogous to 1F, 2F and 4F, respectively, and this was particularly evident on an individual level. The main difference was a fall in the heart rate of about 20 beats per minute in the newborn in each of the three states when compared with their analogous fetal state. We found no equivalent of S5 (crying) in the fetus. The heart rate in S5 was often in excess of 200 beats per minute, and the type of activity and heart rate pattern quite unlike any fetal behavioural pattern. S3 (quiet awake) was only seen in the newborn in association with feeding, and again we found no equivalent behavioural pattern in any of the fetal studies. We conclude that states analogous to quiet sleep and REM sleep are well established in the term human fetus and can be distinguished using ultrasonographically recorded parameters. These two states comprise about 85% of the behaviour exhibited by the healthy term fetus, while episodes analogous to wakefulness occur infrequently. We found no equivalent of quiet awake and crying states pre-natally and we postulate that these are post-natal adaptations to extrauterine existence.

Funded by grant No A/8/1465 from Action Research for the Crippled Child.

Reference

NIJHUIS, J. G. et al, 1982. Are there behavioural states in the human fetus? *Early Human Development*, 6, 177–195.

Book reviews

Pediatric Neurology and Neuroradiology, Cerebral and Cranial Diseases. By Claus Diebler and Oliver Dulac, pp. xv + 408, 1987 (Springer-Verlag, Berlin), DM 298.
ISBN 3-540-15325-X (Berlin)

0-387-15325-X (New York)

The authors' stated aim was to produce a book that was "a synthesis of clinical, pathologic, and radiologic approaches to cranial and cerebral diseases...needed by both the paediatrician and the radiologist". In this the authors, a paediatric neurologist and a neuroradiologist, admirably succeeded, providing an excellent, authoritative and comprehensive text successfully combining the clinical, radiological, developmental and pathological aspects of paediatric neurological diseases.

The book is a result of a 12-year collaboration between the authors and is not only a review of the literature but also their personal experience.

The contents are divided into eight major sections covering cerebral and cranial malformations, neurocutaneous syndromes, inherited metabolic diseases, infectious diseases of the CNS, vascular disorders, intracranial tumours, cranial trauma and miscellaneous conditions. Each section is clearly set out with numerous sub-headings. The clinical features are discussed in detail, supplemented by the necessary embryological and pathological details. The entire text is very informative and there are no major omissions.

Each page is divided into two columns and is liberally interspersed with sub-headings resulting in short sections making it a very readable and well produced book. The references are up to date and are interspersed throughout the text at the end of each section and not at the end of each chapter. This avoids long lists of references and makes it an excellent and rapid source of information for a small group of conditions.

The text is liberally illustrated, groups of illustrations appearing at the end of each section following the references. The illustrative material is almost exclusively computed tomography (CT), reflecting the authors' experience, which is extensively drawn on throughout the text. Some conditions, however, are excessively illustrated and are anecdotal. The legends are very informative and supplement the text. Overall the quality of the CT illustrations was disappointing, but the examples chosen clearly demonstrate the abnormalities. Readers may find the grouping of the illustrations unsatisfactory, resulting in frequent cross-referencing with the text. In the grouping of the illustrations the book resembles the layout of a journal, which somewhat detracts from its main role as a treatise of paediatric neurology.

An accurate and comprehensive subject index is found at the end of the book.

The lack of magnetic resonance imaging (MRI) in the text and in the illustrative material is a serious drawback but is inevitable as the book reflects the authors' combined experience over a 12-year period. This deficiency is not compensated for by the excellence of the clinical and conventional neuro-radiological CT text. Up-to-date practising neuroradiologists and paediatricians will find this a serious limitation.

The book is expensive and its reliance on CT will restrict its appeal. Despite this, it is an excellent source of reference for both paediatricians and neuroradiologists and should be a necessary purchase for respective departmental use.

W. ST C. FORBES

Radiographic Anatomy: A Working Atlas. By Harry W. Fischer, pp. xviii + 205, 1988 (McGraw-Hill, New York), £21.75.

ISBN 0-07-021089-6

This will prove to be a very useful book for medical students and people starting their radiographic or radiological careers (e.g. Part I FRCR candidates). It has no text; just images with accompanying line drawings. Indeed the quality of the contributions by Alyce Norder and John Allen, who prepared the line drawings, has considerably helped make this book the success that it is. The excellent line drawings *actually* do marry with the images. They are also very clear without too much extraneous information. Dr Fischer, for his part, has chosen to demonstrate only the more important features on each image. Thus the newcomer to radiology will not feel swamped by a mass of detail.

It is hard to find points on the negative side of the balance sheet. Whilst the quality of the magnetic resonance images is about par for the course at the time of preparation, some of the computed tomographic images seem a little dated. For practice in the UK there is too much emphasis on oblique chest radiographs and lymphangiography. The omission of ultrasound images is explained in the preface; most students find them very confusing. Likewise neuroanatomy is dismissed as a separate discipline which is "taught as a separate course in most medical schools". So much for jacks of all trades!

Overall this is a very well produced book although it is not quite so comprehensive as Weir & Abrahams' *Atlas of Radiological Anatomy*, which will be its chief rival. This book is not aimed to be all embracing; it is designed for medical students rather than those training in radiology. It may prove to be expensive for medical students. Nevertheless many practising radiologists should welcome a close perusal; it offers a painless chance to refresh our memory of the anatomy of those parts of the body not often reached in day-to-day work.

ADRIAN DIXON

Pediatric Imaging for the Technologist. Ed. by D. M. Wilmot and Gail A. Shako, pp. xvii + 285, 1987 (Springer-Verlag, New York), DM 208.

ISBN 0-387-964398-8 (New York)

3-540-964398-8 (Berlin)

The combination of clearly defined radiographic technique, together with explanations of variations in the anatomy and pathology found in the paediatric patient, will assist the radiographer or trainee radiologist in understanding the reasons why modifications in technique are sometimes required in paediatric practice.

It is always difficult to decide what should be routine views in any department; however, at times I felt that too many views were classified as routine.

The section on the paediatric patient contains useful summary charts relating to child development and psychology. These charts may be of considerable benefit to those who are unused to performing radiological examinations regularly on children. It is pleasing to see that the needs of both parent and child are considered throughout the book.

The sections on immobilization and radiation protection are clear and simple, providing much helpful advice.

The sections on technique are clearly presented and are easily found for quick reference. Good use has been made of illustrations to supplement the text.

This very readable book would be a very useful addition to the paediatric section of any radiographic library. Unfortunately the price will almost certainly preclude it as a text for individual radiographers or students.

ROSEMARY DENNETT

Genitourinary Ultrasound. A Text/Atlas. By Beverly G. Coleman, pp. xviii + 542, 1988 (Igaku-Shoin, New York), £52.00.

ISBN 0-89640-130-8 (New York)

4-260-14130-9 (Tokyo)

Unlike many books emanating from the US, this multi-author tome has only seven contributors, its editor and main contributor being Beverly Coleman. It purports to be a text (exactly what is a text?) as well as an atlas. Ultrasound is a lot easier to write about than to illustrate. Images are in real time and vary considerably with differing gain, brightness and contrast settings, which are adjusted to suit the operator's perception of what a good image should be. Ultrasound illustrations in books are but a spot film of a dynamic process. This book has attempted to get around this problem by accompanying each individual image with three drawings, one an exact replica of the scan, which is annotated, one an anatomical drawing, not annotated, and a line drawing depicting how and where the scan was obtained. This manoeuvre makes the ultrasound images intelligible to most, if not all, potential readers.

The book is in 12 sections covering normal anatomy, variants, chapters on upper and lower tract, retroperitoneal, scrotal, prostatic, childhood and fetal disorders with smaller sections on endosonography and interventional techniques. Each section is preceded by a short, relevant introductory text followed by images of various abnormalities. In addition to the artists' drawings, each image is accompanied by "reading points" which briefly discuss the pathogenesis, clinical significance and ultrasound appearances. These points are referenced.

The book adheres strictly to its title and at no point is any other imaging technique illustrated or discussed. This is to its credit. On the downside, not all the images are on the same page as the annotated drawings, nor are the legends to some annotated images; this book involves a lot of turning pages back and forth. It is a thoroughly enjoyable book to read, is refreshingly to the point with virtually no waffle and is beautifully illustrated. It deserves a place on departmental bookshelves for radiologists, radiographers and perhaps most importantly the ever increasing number of urologists who have decided to eschew their radiological colleagues and practise their own ultrasound.

DAVID RICKARDS

Dynamic Radiology of the Abdomen. Normal and Pathologic Anatomy, 3rd edn. By Morton A. Meyers, pp. xvi + 507, 1988 (Springer-Verlag, New York), DM 248.

ISBN 0-387-96624-2 (New York)

3-540-96624-2 (Berlin)

The third edition of this well known book contains 5% more illustrations and 25% more pages than the previous edition. Nearly 25% of the illustrations are completely new and many of the previous diagrams have been redrawn.

When it first appeared, *Dynamic Radiology* offered a new approach to the understanding of abdominal pathology answering not only "What is it?" but also "how?" and "why?"

The introductory atlas presents full colour anatomical cross-sections of the abdomen and pelvis complemented by labelled tracings. Subsequent chapters deal with the diagnosis and

pathways of spread of infection, malignancies and fluid within the intra- and extraperitoneal spaces. Emphasis is placed on the specific localizing features based on anatomical planes, recesses and the dynamic extension of disease. Further developments in the understanding of the intraperitoneal spread of infection and malignancy from computed tomography (CT) observations have been included in this new edition published 6 years after the previous one. In addition, major developments in the precise evaluation of the extraperitoneal fascia and spaces have also been included. There are extensive references.

Each theme is extensively illustrated by plain radiographs, barium or contrast studies, CT and line diagrams. Ultrasound, isotope scans, magnetic resonance imaging and arteriography are only occasionally used to supplement the other imaging techniques. The text is concise and easy to read.

The quality of the illustrations and general format of the book is of a very high standard and the author undoubtedly achieves his objective admirably.

The British reader will find the paucity of ultrasound images strange; however, the imaging techniques that are used succeed in conveying the dynamic principles involved with clarity and understanding. The lack of ultrasound is also justified because there is no attempt to cover solid organ pathology, except where it impinges on the intra- and extraperitoneal spaces.

This book enhances one's understanding of intra-abdominal pathology to a major degree. I have used the previous edition extensively and never regretted buying a personal copy. I suggest that space should be found for this new edition in all departmental libraries and all those with a particular interest in the abdomen should consider purchasing an individual copy. At around £83 it is not cheap—but then quality never is!

S. B. FIELD

Benign Strictures of Bile Ducts. By Edward I. Galperin, Nicholai F. Kuzovlev and Suren R. Karagiulian; translated by Vladimir Bobrov and Boris Mecrovich, pp. xii + 345, 1987 (International Universities Press, Madison, Connecticut), \$60.00.

ISBN 0-8236-0494-2

This detailed book must be the definitive treatise on benign strictures of the biliary system. The authors' experience is based on treatment of 229 such strictures and this must be the largest series published to date.

The emphasis, however, is very much on the surgical techniques that are utilized with detailed descriptions of the methods employed in the operating theatre. There are no photographs but the text is illustrated by a number of line diagrams. The chapter headings illustrate the thrust of the text, i.e. "preoperative preparation", "operations on scarred bile ducts", etc.

The foreword is written by Henry Pitt, an eminent hepatobiliary surgeon from the United States, in which he suggests that the book will be of interest to radiologists as well as surgeons. Your reviewer would take some issue with this viewpoint. There is little within this book that will be of direct interest to radiologists and the design of the presentation makes reference to a particular point cumbersome. In summary this is a personal text written by a surgeon with unique experience in this specialist field for the benefits of other surgeons who may have a similar interest but who have been denied the clinical material.

It does not have a place in the X-ray department, but for those radiologists who require a wide background knowledge of the problems of bile duct surgery, then this book is available in the library of the British Institute of Radiology.

HENRY LOOSE

Contemporary Issues in Gastroenterology, Vol. 7. Gastrointestinal Nuclear Imaging. Ed. by Michael G. Velchik and Abass Alavi (Guest Eds); Sidney Cohen and Roger D. Soloway (Series Eds), pp. xiv + 289, 1988 (Churchill Livingstone, New York), £45.00. ISBN 0-443-08456-4

This text is aimed at providing a concise account of the various procedures currently adopted in the application of radioisotope techniques to gastroenterology. There are 12 chapters covering a wide range of topics starting with salivary scintigraphy and including topics of interest to gastroenterologists and radiologists such as gastrointestinal transit and reflux studies, gastrointestinal bleeding, localization of ectopic gastric mucosa, liver and spleen scintigraphy, hepatobiliary scintigraphy and abscess detection. Chapters on single photon emission computed tomography and paediatric gastroenterology are included. Opening with a chapter on salivary scintigraphy may not be the ideal way of exciting the interest of gastroenterologists and radiologists in this book, but I can assure you that there are topics of much greater interest and relevance dealt with in subsequent chapters.

It is clear that this book is aimed at the gastroenterologist, to whom it conveys the scope of scintigraphic procedures, and also at the radiologist and nuclear medicine physicians who may consult it to obtain details of how some of the individual procedures may be carried out. The indications, limitations and advantages of each technique are dealt with in each section.

Wherever relevant the physiology, pathophysiology and anatomical considerations are well presented. Data acquisition is also briefly covered in the various sections. The ability of radioisotope procedures to evaluate the normal or deranged function of the gastrointestinal tract is well emphasized.

Although plenty of illustrations have been included, the quality of the illustrations could certainly have been improved. The figures chosen serve to illustrate the points made in the text and the legends are concise and to the point.

Criticisms may, however, be levelled at this book. It is intriguing as to why a chapter on inflammatory bowel disease has not been included in this volume. Only a brief mention is made of this topic, which is of interest to gastroenterologists, in the section on abscess detection. Indium-labelled white cell techniques are well established for this purpose and there are several centres in which this technique is established and widely used. Many readers would be disappointed with this omission. It possibly warranted greater attention than that received by salivary scintigraphy.

Although the coverage of the topics is very relevant to the title of the book and the major aspects of the scintigraphic techniques are covered, it is probably a significant drawback that greater attention is not paid to the relative role of gastrointestinal scintigraphy in comparison with other imaging modalities in the investigation of gastrointestinal disease. This aspect has been poorly researched by many of the authors. The section on chronic cholecystitis in the chapter on hepatobiliary scintigraphy serves to illustrate this point. Ultrasound is claimed to be more expensive and a suggestion is made that oral cholecystography should be performed initially and that ultrasound may be reserved for cases of non-visualization of the gallbladder. This would be to say the least controversial and may, in fact, mislead some of the highly traditional gastroenterologists.

In spite of these criticisms the book deals very well with the nuclear medicine procedures adopted in gastroenterology and would be a valuable addition to a library. I would also recommend it as an easy reference book for those radiologists who wish to obtain a quick overview of a technique, its uses

and limitations when confronted with a request for a particular procedure.

A. E. A. JOSEPH

Non-invasive Diagnosis of Peripheral Vascular Disease. Ed. by W. Robert Felix Jr, pp. xv + 249, 1988 (Raven Press, New York), \$71.00.

ISBN 0-88167-342-0

Vascular radiologists, and vascular surgeons including this reviewer, will welcome this volume on the non-invasive diagnosis of peripheral vascular disease. It is small by the standard of radiological texts, with only 250 pages, and the contributors are mainly surgeons. However, these features in no way diminish its relevance and importance for departments of radiodiagnosis. This book covers the use of ultrasound and related techniques to diagnose occlusive atheroma of the lower limb and carotid arteries, and in venous disease to detect thrombi and valvular incompetence. There are also chapters on the principles of Doppler and duplex ultrasound instruments, and useful practical advice on setting up a non-invasive vascular studies unit.

Few vascular patients now reach the X-ray department without preliminary ultrasound tests to show the presence and severity of disease. The angiogram is more than ever the road map to guide a radiological or surgical intervention. So in the case of lower limb arterial disease, suitability for balloon angioplasty may be virtually assured before the procedure and groin arterial punctures planned accordingly. In respect of carotid disease, the atherosclerotic plaque and its suitability for endarterectomy are now so well shown by duplex scanning that the arteriogram as a diagnostic step is now being omitted in selected cases. As interventional vascular radiology grows, more vascular laboratory instruments will appear in the angiogram suite to fulfil the need for objective measurements.

For example, there may be a pressure gradient across an iliac artery stenosis, irrespective of the significance of its image. Effective balloon angioplasty should abolish the gradient as well as clearing the stenosed arterial segment. There should be a sustained improvement in the overnight distal limb Doppler signals, otherwise a repeat angioplasty may be needed.

This book covers all these issues, and much more. Its strengths include the contributions from Strandness' group on duplex scanning of carotid arteries, and Yao on the Doppler evaluation of lower limb ischaemia. The editor has a useful chapter on the ultrasound diagnosis of deep vein thrombosis. It is an anthology of some of the best American work in the field, and can be recommended without reservation.

ROGER N. BAIRD

Coronary Angioplasty. By David A. Clark, pp. xiii + 198, 1987 (Alan R. Liss, New York), £45.15; \$55.00. ISBN 0-8451-4203-5

This book is a work of art! The book is designed to cover the practical aspects of present day coronary angioplasty and deals particularly well with all the recent advances in angioplasty with an especially good chapter on rapidly growing fields of percutaneous transluminal coronary angioplasty (PTCA) in acute myocardial infarction.

There are other chapters on recurrent stenosis following successful PTCA and complications of coronary angioplasty, and these are entirely rational and easily readable. The four chapters on complex PTCA deal with multiple-vessel disease, total occlusions, bifurcation lesions and bypass grafts. These chapters cover the subjects extremely well. The diagrams throughout the book are clear, well labelled and of the highest quality.

I would like to see in any future edition a chapter dealing with the design and function of an entire angioplasty department, which would include a discussion on the radiology equipment, beds and intensive care beds used for angioplasty, staffing levels, and research.

On balance, this book is extremely good value.

PHILIP GISHEN

Ultrasonography of the Spleen. Ed. by Jean-Noel Bruneton, pp. xvi + 89, 1988 (Springer-Verlag, Berlin), DM 108.

ISBN 3-540-18595-X (Berlin)

0-387-18595-X (New York)

A textbook devoted to sonographic imaging of the spleen alone might appear difficult to justify, and indeed to fill. This 89-page book from Springer-Verlag contains much more than sonography alone and in its production, Jean-Noel Bruneton and Springer-Verlag have completed probably the most thorough and up-to-date review of splenic anatomy, congenital malformation and pathology.

The format is conventional but the detail included by the 18 contributors is exhaustive. One hundred illustrations, which are, of course, predominantly sonograms, more than adequately illustrate the normal and abnormal anatomy described in the text. Almost 40% of the content is devoted to two chapters on the anatomy of the normal spleen, normal anatomic variants, pitfalls and congenital anomalies. Seven major categories of congenital anomaly are described and anyone in search of a reference to the radiology of situs inversus or asplenia need look no further than this little book. A thorough reference is made here, as elsewhere in the book, of relevant comparative imaging techniques.

The remainder of the book is devoted to the ultrasound of splenic trauma, tumour, infection and infestation. Almost all are accompanied by good-quality representative illustrations. Each chapter is independently referenced and the book is completed by a full subject index. The translation would appear to be faultless.

This is not a book that needs to be purchased by every ultrasonographer or radiologist. It does not, however, have any competitor as far as I am aware and provides such an all-encompassing review of this forgotten organ that the capital outlay involved in its purchase for the department library can be fully justified.

D. M. KING

Thyroid Cancer. Its Epidemiology, Clinical Features and Treatment. By Georg Riccabona, pp. x + 150, 1988 (Springer-Verlag, Berlin), DM 98.

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0-387-16555-X (New York)

Thyroid cancer is a rare but particularly interesting disease since it is one of two tumours amenable to therapy using a

radiolabelled element or compound that is actually metabolized by a tumour. Thus when a patient does appear with suspected or proven thyroid cancer it is valuable to have a concise book to which one can refer for the main points in diagnosis and therapy. This book is based on the practical experience of the author and his medical and surgical colleagues on a series of 1943 patients seen between 1956 and 1984. The large number of patients in the series reflects the incidence of goitre in Austria and the special interest of the University Department of Innsbruck in thyroid disease.

The book commences with an interesting review of the epidemiology of thyroid cancer discussing the incidence in different countries (varying by a factor of 10), the incidence in single nodules, and the relation of the disease to endemic goitre, autoimmune disease and other factors. The pathology of the various forms of thyroid cancer is described and the classifications discussed and compared. An interesting review of the aetiology of thyroid cancer includes the investigation of four married couples who developed the disease. No linking features were found.

The diagnostic section is comprehensive, covering nuclear medicine, ultrasound and computed tomography (CT). The value of thyroglobulin assays while on replacement hormone therapy is perhaps underemphasized since this approach will almost certainly replace routine whole-body imaging post-therapy. It is unfortunate that the latest work on FDG imaging is missing since this promises to be a major advance in diagnosis and prognosis.

The section on therapy includes the surgery, chemotherapy and radiotherapy of the disease. The use of desired radiation doses to ablate the thyroid or metastatic disease is confusing when we know that in practice it is difficult to estimate such doses. Otherwise this chapter gives a useful guide to the treatment of thyroid cancer in its various forms.

The book ends with comments on the follow-up of thyroid cancer. In line with modern worries about cost effectiveness and radiation hazards it is nice to know that doing nothing costs about 36 000 DM (including state pensions) while active treatment producing a survival of 10 years costs 33 000 DM.

Experts in the treatment of thyroid disease will be familiar with most of the contents of this book and no doubt will disagree with some parts of it. Overall, however, it is an accurate summary of the present facts and therefore will be of value to trainees and especially of value to physicians who are unfamiliar with thyroid cancer. There are many small errors in spelling but these are unimportant. It would have been valuable, however, to include images of the classical appearances of the four main thyroid cancer histologies and perhaps, to avoid confusion, to relegate the diagnosis and treatment of medullary cancer of the thyroid to a completely separate section. The book is up to date and good value for money and should be in most medical libraries.

RALPH MCCREADY

The British Journal of Radiology

Review article

The linear-quadratic formula and progress in fractionated radiotherapy

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Clinical gains have been reported from the use of non-standard fractionation schedules planned with a radiobiological basis. Hyperfractionation provides the leading example, as described below, with accelerated fractionation being developed more recently. Although examples of almost every kind of fractionated schedule can be found in the literature over the past 90 years, it is only within the last decade that the biological factors concerning overall time and delayed proliferation after irradiation, and the effect of dose per fraction, have been understood. Both these factors operate differently on late- and early-reacting tissues, because cell proliferation in late-reacting tissues is slow or absent, but early reacting tissues and tumours depend upon cells that proliferate rapidly. This basic knowledge is still diffusing through the radiotherapy community and I hope this review will help the diffusion process. The biological factors concerning fractionation seem to apply to the majority of tissues and tumours, so that new schedules can be planned that are effective in practice.

Attempts to deal with hypoxic cells in tumours or to use high-linear-energy-transfer (LET) radiation have been less generally successful, probably because in those strategies we need to identify subpopulations that are smaller. Tumours that are resistant to conventional radiotherapy because they contain hypoxic cells and do not reoxygenate cannot be identified yet. Tumours with a high intrinsic relative biological effectiveness (RBE) might be identifiable if rapid assays of radiation response are confirmed as reliable (Brock et al, 1986; Peters et al, 1988b), but they are apparently a smaller proportion of all tumours than those that respond predictably to changes in dose fractionation using conventional low-LET radiation. The new assays of proliferation rate in human tumours using bromodeoxyuridine (BUDR) or iododeoxyuridine (IUDR) as a tracer and flow cytometry should enable accelerated fractionation to be applied to individually selected tumours before long. It is of great interest to the present author to see these developments; it was the

study of fractionated irradiation that brought me into radiobiology over 30 years ago (Mitchell, 1953; Fowler & Stern, 1960).

Perhaps the most important step forward in fractionated radiotherapy was the French discovery that rather small daily fractions over a period of about 6 weeks gave a good ratio of local control to both early and late complications in normal tissues (Coutard, 1932; Baclesse, 1958). ("Daily" to them was 6 days a week. A 5-day week leaves intervals of 72 h over each weekend.) This success is now well explained by the fact that 6 weeks is long enough to allow accelerated compensatory proliferation in skin and mucosa to ameliorate acute reactions, and that the doses per fraction of only about 2 Gy keep the late reactions from being excessive. The radiotherapists who designed these schedules chose the total dose levels wisely so as to balance the three factors of local control, acute reactions and late complications. A different strategy has also been successful and, until recently, it has not been possible to sort out why, *i.e.* the short schedules used in Manchester of 16 fractions in 21 days (Paterson, 1963). This success can now be interpreted in terms of fast proliferation in a substantial proportion of tumours, perhaps half of them, with, for example, doubling times of only ~4 to 6 days in head and neck cancer. Lower total doses are necessary both in order to keep acute reactions tolerable (because of the short overall time) and to keep late complications acceptable (because of the rather large doses per fraction of 3.4 Gy). But if—and only if—tumorigenic cells double in number in only 4 to 6 days during treatment, then such accelerated schedules can indeed compete with 30 or even 35 fractions of 2 Gy doses in 6 or 7 weeks, as explained in detail below. The traditional arguments between proponents of either strategy are no longer necessary, and improvements can be considered for both these types of schedule.

The currently reported clinical gains from non-standard fractionation come from hyperfractionation schedules using two small fractions per day in Europe

(Horiot et al, 1988; $70\text{F} \times 1.15\text{ Gy} = 80.5\text{ Gy}$ in 7 weeks) and in the USA (Parsons et al, 1988; $65\text{F} \times 1.2\text{ Gy} = 78\text{ Gy}$ in 6½ weeks). Both these schedules are reported to give 10 to 15% more local tumour control than the control arm ($35\text{F} \times 2\text{ Gy} = 70\text{ Gy}$ in 7 weeks) with no extra late complications, exactly as predicted on radiobiological grounds (Thames et al, 1983).

At the other extreme from hyperfractionation is the continuous hyperfractionated accelerated radiation therapy (CHART) schedule of Saunders et al (1988), which employs 36 fractions of 1.5 Gy, equal to 54 Gy in 12 days continuously, without stopping at the weekend. Daytime intervals of 6 h are maintained. Is the lower total dose compensated for by the shorter overall time? We describe in this review some new and potentially precise ways of making such comparisons; precise, but dangerous if wrong parameters are chosen.

Between these extremes, many recently designed protocols make use of both acceleration and hyperfractionation to give high doses in somewhat shorter times than 6 to 7 weeks. We shall compare some of them critically in the present review.

Both hyperfractionation, defined as smaller doses than 1.8 Gy per fraction, and acceleration, defined as shorter overall times than 6 or 7 weeks, require the use of two or three fractions per day, specifically to avoid extending overall times and allowing tumours to proliferate even more, and to avoid doses per fraction above 2 Gy. With the presently recommended minimum daytime interval of 6 h, it is not likely that more than three fractions per day can be given in practice. Even this schedule requires reorganization of the radiotherapy department's working habits. However, two fractions per day should be within any department's capabilities, especially because not all the patients would require such non-standard schedules. We are not talking about palliation, where corners can be cut to save time, especially the patient's time.

The basic advances in modern radiobiology

Was it a coincidence that the current successes with modern radiotherapy schedules should have arisen soon after the linear-quadratic (LQ) formula came into widespread use in the early 1980s? Not really, because the LQ formalism has undoubtedly speeded up the understanding and application of the new knowledge about dose-per-fraction effects.

Three basic steps can be defined in shaping the current views of the biological factors involved in radiotherapy. Each of them has depended fully on results of animal experiments, and then upon confirmation from clinical observations.

Overall time: late vs early reactions

Late reactions occur, by definition, in tissues whose cell populations proliferate so slowly that the proliferating compartment does not renew itself for several months, even a year or longer. This is because cells do not die after irradiation until they try to divide.

Only after that time does compensatory proliferation speed up in the damaged tissue. Radiation has this unique property, which is different from drugs, heat or trauma. Therefore, in late-reacting tissues, no compensatory proliferation occurs during the weeks of radiotherapy. The practical point is that overall time in radiotherapy can be doubled or halved with no change required in total dose, and with no change in late complications if the total dose is not changed.

This point emerged during the late 1970s from the work of cell kineticists such as Denekamp (1973, 1982), Hegazy and Fowler (1973), Denekamp et al (1976) and Stewart et al (1980), who identified the population turnover time as the start-up time for accelerated compensatory proliferation, using tritiated thymidine autoradiography. For example, there was a difference between the sole and the instep of mouse feet, the skin on the sole having a faster turnover time than that on the instep, and, therefore, an earlier response to radiation. This was followed by the same general conclusion, but after 10 months instead of 10 days, in mouse bladder (Stewart et al, 1980). All of this then appeared so obvious that many readers said "of course" and forgot about it again.

The practical point concerning acute or early reactions is that they can be reduced or avoided by prolonging radiotherapy (and this is partly why schedules as long as 6 or 7 weeks are popular), yet the late reactions will *not* be reduced or avoided. Basal layer cells of the skin and mucosa can accelerate from their normal turnover time of 7–10 days (in pigs and men; 5 days in mice) to doubling times of only 1–2 days towards the end of a 6-week radiotherapy schedule. This means that extra dose can be added at 9 or 10 Gy per week, without much worsening of the acute reactions, indeed sometimes with re-epithelialization in progress. Radiotherapists have certainly exploited that. It has two dangers. One is that late effects are not spared, and will respond to the accumulated total dose in due, unavoidable, proportion. The other danger is that some tumours, not all, may be proliferating almost as fast as the normal skin or mucosa. It is in effect a race being run between the tumour cells and the normal cells with only one horse being observable—the mucosal or skin reactions. Too much prolongation means loss of tumour control, although it is undoubtedly comfortable for the patient.

Although these truths seem self-evident now, they were not perceived or understood as recently as 1978. Overgaard et al (1988) recently described the design of a protocol to improve the radiotherapy of carcinoma of the larynx in Denmark. In 1978, a 3-week split was introduced together with a dose escalation from 60 to 72 Gy, using the rationale that normal tissues proliferate faster than tumours. They were surprised when the late reactions then became more severe, and reduced the total dose to 68 Gy. The tumour control then fell from 72 to 60%. These clinical results are entirely consistent with the teachings of modern radiobiology as summarized here. Indeed, they provide rather classical

confirmation of the bad effect of prolongation. In particular, the 3-week split required an additional 12 Gy to keep the local control constant (*i.e.* 50 cGy per day), but doing this caused a higher incidence of late oedema and fistula (Overgaard et al, 1988).

A corollary is that acute reactions (and effects on the tumour) will become stronger if overall time is reduced, unless the total dose is reduced. Whilst nominal standard dose (NSD), time, dose and fractionation (TDF) and cumulative radiation effect (CRE) were intended to give guidance about how much to reduce total doses in shorter and sharper schedules, these formulae had a wrong balance between the effects of time and dose-per-fraction, which came out badly for late effects, although not too badly for acute reactions. Nominal standard dose, TDF and CRE overestimated the effect of overall time on late reactions and underestimated it on early reactions (see below). They should no longer be used.

It was the cell kinetics people who unravelled the difference in response of early and late reactions to overall time (Denekamp, 1973, 1982, 1986; Tubiana, 1988). It is rates of cell proliferation which should be used to replace the formalized $T^{0.11}$ etc. power terms intended to represent the effect of overall time.

It was always a theoretical possibility that prolonging overall time would lead to loss of tumour control, because of too much proliferation in the tumour. This hazard was well documented in mouse tumours (Suit et al, 1977; Denekamp, 1982, 1986; Fowler, 1983, 1986; Trott & Kummermehr, 1985). But everyone knew that mouse tumours doubled in size every few days whilst human tumours take several weeks or months—so why worry about whether treatments take 3 weeks or 7? Or even longer if a split keeps the patient comfortable?

Again, the answer has been available for a long time in tumour kinetics data (Steel, 1977; Meyer, 1981). But it was not emphasized until clinical results were analysed of radiotherapy schedules in which the overall time was varied, with sufficient constancy of other parameters (usually acute effects) to be able to determine the loss of tumour control with extension of overall time (Parsons et al, 1980; Overgaard et al, 1988).

Fowler (1986) reviewed these data and found doubling times of the tumorigenic cells, in clinical practice, to be 3 to 8 days (head and neck tumours 3 to 7 days). This empirical approach makes no assumptions about cells kinetic parameters. It might be a coincidence that these doubling times come out to be closer to the "potential doubling times" (cycle time $\times \log_2$ divided by growth fraction) than to the cell cycle time or (especially) to the volume doubling time. Withers et al (1988) have published a larger review with the same conclusion: tumour cells double in number every 3 to 4 days on average (with a large spread), at least in the last half of a 3- or 4-week schedule of radiotherapy.

These empirical doubling times are given fresh emphasis by the recent use of flow cytometry to measure potential doubling times of individual human tumours within a day of taking a biopsy (Begg et al, 1985). This

Table I. What's wrong with NSD, TDF and CRE?

1. The fraction number factor
 - (a) $N^{0.24}$ does not predict the severe late damage that occurs for larger fraction sizes.
 - (b) The graph of total dose against number of fractions is curved, not straight (log-log).
 - (c) Fraction size, not number, is the important parameter.
2. The time factor
 - (a) $T^{0.11}$ predicts a large increase of isoeffect dose at first, then increasing more slowly. The biological fact is just the opposite: it shows no increase at first and then a rapid rise of isoeffect dose as proliferation accelerates.
 - (b) The time factor is underestimated for tumours and acutely reacting tissues.
 - (c) The time factor is overestimated for late-reacting tissues.
3. General

Time, dose and fractionation tables are too easy to use without thinking about late/early reactions or proliferation rates.

technique uses BUdR or IUdR as a tracer for DNA synthesis instead of tritiated thymidine, with monoclonal antibodies to make the cells in S-phase fluorescent. If the biopsy is delayed by 6 h or so after giving the tracer to the patient, an estimate of the potential doubling time as well as the labelling index can be obtained from the single biopsy. This method has shown a range of potential doubling times from ~2 to 25 days with a median value of ~5 days. This is short enough to be worrying in a substantial number of human tumours (Begg et al, 1988; Wilson et al, 1988).

Dose per fraction: late vs early reactions

It was Dr Withers who perceived most clearly the essential difference between the fractionation response (at constant overall time) of late and early radiation reactions. He plotted total isoeffect dose against dose-per-fraction and showed that the curves for late reactions were consistently steeper than those for early reactions (Withers et al, 1978, 1982). Whilst this had been known for the central nervous system (CNS) since 1975 (Wara et al, 1975; Sheline et al, 1980), it was not interpreted properly because of the misleading focus on fraction number instead of fraction size at that time. The interpretation was given a quantitative basis by Thames et al (1982) and applied to the immediate question of planning improved radiotherapy protocols before 1983. It is from this work that a more conscious attempt to use hyperfractionation stemmed, with the good clinical results now being reported. Indeed, the reported increase of 10 to 15% in local control is precisely as predicted by radiobiological calculations using the linear-quadratic theory (Thames et al, 1983; Fowler, 1984a).

The linear-quadratic formula

First, what's wrong with NSD, TDF and CRE, etc.? Table I lists the factors involved. Perhaps the main one

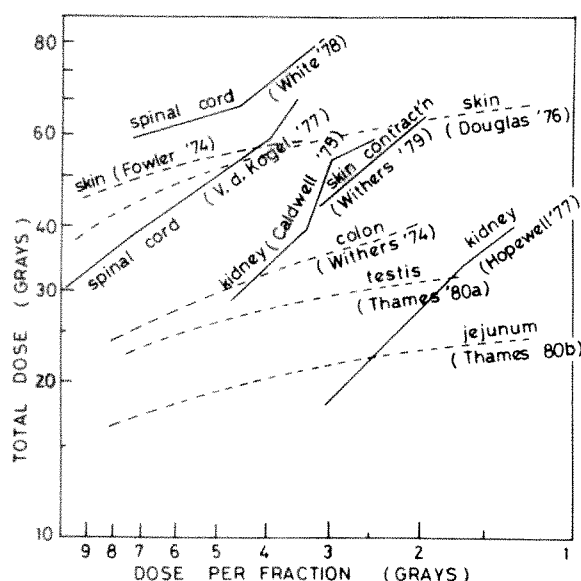


Figure 1. Total doses to give equal biological effects in fractionated schedules against size of dose per fraction for experimental animal systems (redrawn from Withers et al, 1982). Late effects (solid lines) require larger changes in total dose than early effects (dotted lines) when dose per fraction is changed.

is the availability of easy-to-use tables that have discouraged clinicians from thinking about the real biological factors involved. It is time to retire NSD, TDF and CRE to an honoured place in a historical museum (Ellis, 1969; Kirk et al, 1971; Orton & Ellis, 1973). These formulae should no longer be used to report results of clinical trials except perhaps in relation to early normal-tissue reactions. Yet we are still seeing clinical papers that list TDF and CRE values. It is extremely important to give the real details of any treatment, especially total dose, size or number of fractions and overall time, and not to telescope these into *any* single number, whether based on NSD or LQ.

It is surprising that one of the main factors hindering the acceptance of the LQ approach to working out isoeffect doses has been the alleged absence of a "time factor" in the LQ formula. No time factor *should* be present for late effects. There are now good time factors available for tumours and acute reactions but there is a price to pay. Four parameters have to be specified instead of one (see below). It is surprising that people have felt so attached to a time factor that was wrong, being obviously too large for late effects and not large enough for early effects.

The LQ formula has held up very well over the last decade as new data have come in. Many animal experiments have been carried out to test it, usually where proliferation was avoided to obtain a clear test of LQ (Douglas & Fowler, 1976; Thames et al, 1982; Travis et al, 1983; Fowler, 1984a,b; Stewart et al, 1984a,b; Parkins & Fowler, 1985, 1986; Joiner &

Denekamp, 1986b; Lindenberg et al, 1986). Clinical data have also been obtained that are consistent with the animal values of α/β (Turesson & Notter, 1984; Overgaard, 1985, 1988; Bentzen et al, 1988; Thomas et al, 1988). The range of validity appears to extend from 1 Gy to 8 or 10 Gy, or higher in some tissues such as mouse skin (Fowler, 1984a,b; Joiner & Johns, 1988). The fear that less repair may occur at doses below 2 Gy in CNS has been diminished by the realization that the observations could be explained by lack of complete repair because the fraction intervals were too short (Thames et al, 1988).

The fear that multiple fractions may not each cause the same effect has been removed by five experiments *in situ* (Thames & Withers, 1980; Travis et al, 1983; Fisher & Hendry, 1986; Joiner & Denekamp, 1986a; Fowler et al, 1987) in spite of some experiments *in vitro* that do not confirm that. It may be more difficult to maintain the physiological conditions constant over many fractions *in vitro* than in animals.

The old criticism that the LQ dose-response curves keep on bending and are inconsistent with *in vitro* survival curves that are straight at high doses is irrelevant because LQ is not intended for doses higher than 8–10 Gy, the highest used in radiotherapy. In any case, LQ is simply a low-dose approximation to equations that do become straight exponentials at higher doses (Gilbert et al, 1980; Curtis, 1986).

There is a consistent finding of low values of α/β for late effects with little or no overlap with the higher values for early reactions (see Tables II, III).

Although the reciprocal total dose or Fe plot (Douglas & Fowler, 1976) is not the most accurate way to calculate α/β , it is the easiest method and gives a fairly accurate value if the data are good, but only an optimistic estimate of the error range. The best method is the direct analysis of Thames et al (1986), but this requires individual data from every animal or patient. However, for practical purposes, α/β can be obtained roughly from two schedules if one knows the total doses D_1 and D_2 , which give equal biological effects from the two schedules $n_1 \times d_1$ and $n_2 \times d_2$:

$$E = n_1(\alpha d_1 + \beta d_1^2) = n_2(\alpha d_2 + \beta d_2^2) \quad (1)$$

So,

$$D_1(\alpha/\beta + d_1) = D_2(\alpha/\beta + d_2)$$

Therefore

$$\alpha/\beta = \frac{D_2 d_2 - D_1 d_1}{D_1 - D_2} \quad (2)$$

Some applications of the LQ formula to practical radiotherapy questions are given in this article. Others can be found in the excellent book by Thames and Hendry (1987). There is a difference in these approaches.

The basic formula is:

$$E = n(\alpha d + \beta d^2) \quad (3)$$

Table II. Ratio of linear to quadratic coefficients from multifraction experiments with animals

Reactions	References	α/β (Gy)
<i>Early reactions</i>		
Skin		
Desquamation	Douglas & Fowler (1976)	9.1–12.5
	Joiner et al (1983)	8.6–10.6
	Moulder & Fischer (1976)	9–12
Jejunum		
Clones	Withers et al (1976)	6.0–8.3
	Thames et al (1981)	6.6–10.7
Colon		
Clones	Tucker et al (1983)	8–9
Weight loss	Terry & Denekamp (1984)	9–13
Testis		
Clones	Thames & Withers (1980)	12–13
Mouse lethality		
30d	Kaplan & Brown (1952)	7–10
30d	Mole (1957)	13–17
30d	Paterson et al (1952)	11–26
Tumour bed		
45d	Begg & Terry (1984)	5.6–6.8
<i>Late reactions</i>		
Spinal cord		
Cervical	van der Kogel (1979)	1.8–2.7
Cervical	White & Hornsey (1978)	1.6–1.9
Cervical	Ang et al (1983)	1.5–2.0
Cervical	Thames et al (1988)	2.2–3.0
Lumbar	van der Kogel (1979)	3.7–4.5
Lumbar	White & Hornsey (1978)	4.1–4.9
	Leith et al (1981)	3.8–4.1
	Amols, Yuhas (quoted by Leith et al, 1981)	2.3–2.9
Colon		
Weight loss	Terry & Denekamp (1984)	3.1–5.0
Kidney		
Rabbit	Caldwell (1975)	1.7–2.0
Pig	Hopewell & Wiernik (1977)	1.7–2.0
Rats	van Rongen et al (1988)	0.5–3.8
Mouse	Williams & Denekamp (1984a, b)	1.0–3.5
Mouse	Stewart et al (1984a)	0.9–1.8
Mouse	Thames et al (1988)	1.4–4.3
Lung		
LD ₅₀	Wara et al (1973)	4.4–6.3
LD ₅₀	Field et al (1976)	2.8–4.8
LD ₅₀	Travis et al (1983)	2.0–4.2
Breathing rate	Parkins & Fowler (1985)	1.9–3.1
Bladder		
Frequency, capacity	Stewart et al (1984b)	5–10

Values before 1984 are recalculated from references in Fowler (1984b). Values after 1984 are as quoted in the references listed in the present paper.

where the surviving proportion of cells is given by $S = e^{-E}$; n and d are the number and size of the dose fractions, and α and β are the linear and quadratic coefficients, respectively.

$$E = D(\alpha + \beta d) \quad (4)$$

where D is the total dose ($n \times d$). In order to bring α and

Table III. α/β ratios for early and late end-points in different human tissues (Overgaard, 1985, 1988)

Tissue	End-point	α/β (Gy)
Skin	Erythema	10.5–11.3
	Moist desquamation	10.0
	Late fibrosis	1.9–2.3
	Telangiectasia (Telangiectasia ^a)	5.7 3–5
Lung	Pneumonitis	4.4–6.9
	Fibrosis (later)	3.0–3.6
Bone	Rib fractures	1.8–2.5

^aFrom Turesson & Notter (1984).

β together as a ratio, both sides of Equation 4 must be divided by either α or β . Thames and Hendry (1987) divide through by β :

$$E/\beta = D(\alpha/\beta + d) \quad (5)$$

and this gives them “TE” or total effect, in units of grays squared.

However, I shall maintain the method proposed by Barendsen (1982) who divides through by α :

$$E/\alpha = D\left(1 + \frac{d}{\alpha/\beta}\right) \quad (6)$$

Here the effect level E/α is in units of grays and can be considered a “biologically effective dose”, which is a useful concept and has the dimensions of dose. Barendsen called it the extrapolated tolerance dose (ETD) or, to include tumours and less than full tolerance, the extrapolated response dose (ERD), which has been used by other authors (Dale, 1985). Equation 6 can be written in words:

Biologically effective dose (E/α) = total dose (D)
× relative effectiveness.

The relative effectiveness (RE) is the factor in parentheses, $(1 + d/(\alpha/\beta))$. It too is conceptually very useful. It gives the factor by which the isoeffect dose is less than that for a continuous low-dose-rate (or an infinite number of very small fractions) when that dose per fraction d is used. It is the quickest way to see that total dose must be reduced (and by how much) if larger doses per fraction are used.

Figure 2 explains these relationships. The calculations outlined so far are extremely simple and can be done in one's head or on the back of an envelope—but get a second person to check them. The addition of a time factor is very recent (see next section) but it is correct to have no time factor for comparisons of *late* effects.

Examples

What are the calculated late effects of $30F \times 2 \text{ Gy} = 60 \text{ Gy}$? First, for general late effects, let us assume a value of $\alpha/\beta = 3 \text{ Gy}$, and calculate the

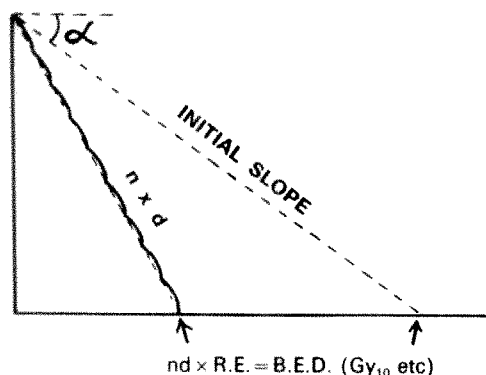


Figure 2. The total effect of n equal fractions is represented by extending the line joining the origin to the survival (or damage) caused by the dose per fraction d . The total effect (level of damage) is the same as if the initial slope α had been extended to the "biologically effective dose (BED)" equal to the real dose multiplied by

$$RE = \left(1 + \frac{d}{\alpha/\beta}\right)$$

(Barendsen, 1982). This relative effectiveness value is an easily calculated measure of the effectiveness of any schedule, depending only on dose-per-fraction d and α/β .

biologically effective dose (BED):

$$\text{Late BED} = E/\alpha = 60(1 + 2/3) = 60 \times 1.667 = 100 \text{ Gy}_3$$

The value of 100 Gy₃ is the biologically effective dose for fibrosis, ulceration or necrosis resulting from the physical dose of 60 Gy given as 2 Gy fractions. The subscript "3" is added first to tell us that this is the *biological*, not the physical dose, and secondly to remind us that a value for α/β of 3 Gy was assumed.

For early (and tumour) effects let us assume $\alpha/\beta = 10$ Gy:

$$\text{Early BED} = E/\alpha = 60(1 + 2/10) = 60 \times 1.20 = 72 \text{ Gy}_{10}$$

It can be seen that if very low dose-rates or ultimate hyperfractionation could be used so that the BEDs would actually apply, the late-reacting tissues would tolerate more dose than the tumours or early reacting tissues. These values of 100 Gy₃ and 72 Gy₁₀ can be considered as "modest standard" values. Biologically effective doses in Gy₁₀ can be compared with any values of Gy₁₀ from other schedules, but not with Gy₃ or values obtained assuming other values of α/β than 10. Similarly, values of Gy₃ can be compared with other values of Gy₃. If obtained from different parts of the same schedule, they can be added or subtracted, provided they relate to the same α/β , just as TDF values could be (Barendsen, 1982).

For example, if we consider a stronger "standard" schedule of 35F $\times$ 2 Gy = 70 Gy in 7 weeks, we obtain:

$$\text{Late BED} = E/\alpha = 70(1 + 2/3) = 70 \times 1.667 = 116.7 \text{ Gy}_3$$

$$\text{Early BED} = E/\alpha = 70(1 + 2/10) = 70 \times 1.20 = 84.0 \text{ Gy}_{10}$$

These values can be considered as "strong standard"

values. They differ from those given above for 30F $\times$ 2 Gy by the differences in total dose multiplied by the RE value (in parentheses), *i.e.* by simple additivity of the biologically effective dose for each value of α/β .

To compare other schedules, we must of course assume the same ratios α/β for each tissue. For example, the EORTC Hyperfractionation Trial used 70F $\times$ 1.15 Gy = 80.5 Gy in 7 weeks (Horiot et al, 1988). We consider the effect of overall time below; here it is equal.

$$\begin{aligned} \text{Late BED} &= E/\alpha = 80.5(1 + 1.15/3) \\ &= 80.5 \times 1.383 = 111.4 \text{ Gy}_3 \end{aligned}$$

$$\begin{aligned} \text{Early BED} &= E/\alpha = 80.5(1 + 1.15/10) \\ &= 80.5 \times 1.115 = 89.8 \text{ Gy}_{10} \end{aligned}$$

We can see that the effect on the late tissues is 11.4% stronger (in effect, *i.e.* proportional to log cell kill) than for 30F $\times$ 2 Gy, which was 100 Gy₃. The effect on tumours should be 25% stronger (*i.e.* 89.8/72). With multiple equal fractions, the effect is proportional to the total dose for a given fraction size. There is, therefore, a predicted therapeutic gain of 12% (1.25/1.11). This illustrates the strategy of hyperfractionation. To compare more precisely with the control arm of the EORTC trial we should calculate the effect of 35F $\times$ 2 Gy = 70 Gy in 7 weeks:

$$\text{Late BED} = E/\alpha = 70(1 + 2/3) = 70 \times 1.667 = 116.7 \text{ Gy}_3$$

$$\text{Early BED} = E/\alpha = 70(1 + 2/10) = 70 \times 1.20 = 84 \text{ Gy}_{10}$$

from above.

It is clear that this control arm is less effective for tumour effects than the 89.8 Gy₁₀ arm just listed, and in addition it appears some 5% more damaging to the late-reacting tissues. This illustrates even more clearly the advantage of using the smaller fraction sizes of the hyperfractionation protocol.

Table IV gives examples of total doses for various fraction sizes calculated for several values of α/β , calculated to give the same late complication rates as the standard schedules shown. These values can be used instead of TDF tables for *late* reactions, bearing in mind the possible variations of α/β .

Continuous low-dose-rates can be dealt with by replacing the dose per fraction d in the relative effectiveness parentheses (Equation 6) by total dose $\times g$, where g depends upon the duration of the exposure in relation to rate of repair of sublethal damage. Values for g can be obtained from Table 6.4 on page 234 of Thames and Hendry (1987).

Incomplete repair between fractions can be dealt with by multiplying the dose per fraction inside the relative effectiveness parentheses by the factor $(1 + h_m)$ where h_m is the fraction of unrepaired but repairable damage remaining from the previous fraction(s). Values of h_m can be obtained from Table 6.3 on page 233 of Thames and Hendry (1987). They work equally well when applied to the second (β) term in the parentheses of either Equations 5 or 6. Table VII and Fig. 8 give some calculated values of the extra damage occurring for various fraction intervals.

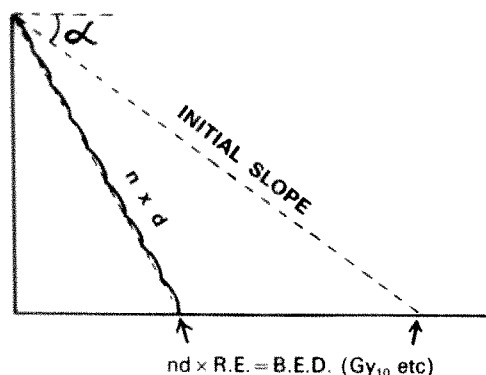


Figure 2. The total effect of n equal fractions is represented by extending the line joining the origin to the survival (or damage) caused by the dose per fraction d . The total effect (level of damage) is the same as if the initial slope α had been extended to the "biologically effective dose (BED)" equal to the real dose multiplied by

$$RE = \left(1 + \frac{d}{\alpha/\beta}\right)$$

(Barendsen, 1982). This relative effectiveness value is an easily calculated measure of the effectiveness of any schedule, depending only on dose-per-fraction d and α/β .

biologically effective dose (BED):

$$\text{Late BED} = E/\alpha = 60(1 + 2/3) = 60 \times 1.667 = 100 \text{ Gy}_3$$

The value of 100 Gy₃ is the biologically effective dose for fibrosis, ulceration or necrosis resulting from the physical dose of 60 Gy given as 2 Gy fractions. The subscript "3" is added first to tell us that this is the *biological*, not the physical dose, and secondly to remind us that a value for α/β of 3 Gy was assumed.

For early (and tumour) effects let us assume $\alpha/\beta = 10$ Gy:

$$\text{Early BED} = E/\alpha = 60(1 + 2/10) = 60 \times 1.20 = 72 \text{ Gy}_{10}$$

It can be seen that if very low dose-rates or ultimate hyperfractionation could be used so that the BEDs would actually apply, the late-reacting tissues would tolerate more dose than the tumours or early reacting tissues. These values of 100 Gy₃ and 72 Gy₁₀ can be considered as "modest standard" values. Biologically effective doses in Gy₁₀ can be compared with any values of Gy₁₀ from other schedules, but not with Gy₃ or values obtained assuming other values of α/β than 10. Similarly, values of Gy₃ can be compared with other values of Gy₃. If obtained from different parts of the same schedule, they can be added or subtracted, provided they relate to the same α/β , just as TDF values could be (Barendsen, 1982).

For example, if we consider a stronger "standard" schedule of 35F $\times$ 2 Gy = 70 Gy in 7 weeks, we obtain:

$$\text{Late BED} = E/\alpha = 70(1 + 2/3) = 70 \times 1.667 = 116.7 \text{ Gy}_3$$

$$\text{Early BED} = E/\alpha = 70(1 + 2/10) = 70 \times 1.20 = 84.0 \text{ Gy}_{10}$$

These values can be considered as "strong standard"

values. They differ from those given above for 30F $\times$ 2 Gy by the differences in total dose multiplied by the RE value (in parentheses), *i.e.* by simple additivity of the biologically effective dose for each value of α/β .

To compare other schedules, we must of course assume the same ratios α/β for each tissue. For example, the EORTC Hyperfractionation Trial used 70F $\times$ 1.15 Gy = 80.5 Gy in 7 weeks (Horiot et al, 1988). We consider the effect of overall time below; here it is equal.

$$\begin{aligned} \text{Late BED} &= E/\alpha = 80.5(1 + 1.15/3) \\ &= 80.5 \times 1.383 = 111.4 \text{ Gy}_3 \end{aligned}$$

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We can see that the effect on the late tissues is 11.4% stronger (in effect, *i.e.* proportional to log cell kill) than for 30F $\times$ 2 Gy, which was 100 Gy₃. The effect on tumours should be 25% stronger (*i.e.* 89.8/72). With multiple equal fractions, the effect is proportional to the total dose for a given fraction size. There is, therefore, a predicted therapeutic gain of 12% (1.25/1.11). This illustrates the strategy of hyperfractionation. To compare more precisely with the control arm of the EORTC trial we should calculate the effect of 35F $\times$ 2 Gy = 70 Gy in 7 weeks:

$$\text{Late BED} = E/\alpha = 70(1 + 2/3) = 70 \times 1.667 = 116.7 \text{ Gy}_3$$

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from above.

It is clear that this control arm is less effective for tumour effects than the 89.8 Gy₁₀ arm just listed, and in addition it appears some 5% more damaging to the late-reacting tissues. This illustrates even more clearly the advantage of using the smaller fraction sizes of the hyperfractionation protocol.

Table IV gives examples of total doses for various fraction sizes calculated for several values of α/β , calculated to give the same late complication rates as the standard schedules shown. These values can be used instead of TDF tables for *late* reactions, bearing in mind the possible variations of α/β .

Continuous low-dose-rates can be dealt with by replacing the dose per fraction d in the relative effectiveness parentheses (Equation 6) by total dose $\times g$, where g depends upon the duration of the exposure in relation to rate of repair of sublethal damage. Values for g can be obtained from Table 6.4 on page 234 of Thames and Hendry (1987).

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0.4 log. per gray. Outside this range tumours would either be incurable or all cured. I have done calculations for 0.2, 0.25, 0.3, 0.35, 0.4, and 0.45 log_e/Gy but shall present only those from the middle of the range.

Having specified α , β is specified if α/β is chosen. It is reasonable to choose $\alpha/\beta = 10$ Gy for rapidly proliferating normal tissues and for tumours (Williams et al, 1985). Higher values of 25 or even 35 Gy could be used for tumours to test the difference. Lower values of α/β for tumours have occasionally been reported (Suit et al, 1989) and indeed might be expected for highly radioresistant tumours such as glioblastomas or some malignant melanomas, but we do not know for sure. Values of α/β below ~ 5 Gy have not been reported for tumours so they are not likely to be confused with late-reacting tissues.

The range of cell proliferation times measured by flow cytometry before treatment is large, from 2 to about 25 days with median values of 4 or 5 days (Begg et al, 1988; Wilson et al, 1988). Flow cytometry measures T_{pot} ($= \log_e 2 \times T_c / \text{GF}$) before treatment. This is only equal to T_p , the effective doubling time, if the cell loss factor falls to zero with no change in the birth rate of the cells. There is agreement from clinical radiotherapy results, which give empirical values of T_p , that average values of the effective doubling time of cells that regrow tumours are 3 or 4 days in head and neck tumours (Maciejewski et al, 1983; Fowler, 1986; Withers et al, 1988). It is expected that prostate tumours would proliferate much more slowly because their labelling indices (LI) are much lower (Meyer, 1981). No conclusions can be drawn from gross volume doubling times alone; cell loss factors can be as large as 99% and in that case, volume doubling times would be 100 times larger than T_{pot} . Whilst some breast tumours have low values of LI,

others have high values (Meyer, 1981). I shall present profiles of tumour response to various fractionated schedules with a full range of assumed doubling times from 2 to 20 days. Even these are average doubling times, assumed constant from T_k to the end, T , of treatment. We do not know enough to specify any possible changes of T_p during treatment or during any gaps. It is necessary to keep clear the distinction between T_p , the effective doubling time, and T_{pot} , the inverse of the doubling rate of cells in the tumour, even though they are obviously similar and might turn out to be identical.

For tumour cell proliferation there are two approaches. Withers et al (1988) have presented data suggesting that tumour cell proliferation does not accelerate until 3 to 4 weeks after starting radiotherapy. Others, including the present author, think that proliferation speeds up as soon as the tumour shrinks, which can be as soon as two or three fractions have been given. Cells in regions of poor nutrition would then become closer to the capillary supplies, so that the growth fraction could increase. To deal with this uncertainty, two calculations are presented below, one assuming proliferation constant from T_k to T and the other throughout treatment from 0 to T . Whilst these assumptions alter drastically the level of cell kill calculated, they have less effect on the relative effectiveness of various schedules, which is our present question.

Applications of the LQ with time factors

How much effect is lost by proliferation in tumours?

The first application is to ask what proportion of the cell killing effect of radiotherapy is lost if cells proliferate at any assumed rate during treatment. Of

Table V. Estimated log cell kill in tumours, including proliferation, for some current fractionation schedules

Schedule	Log ₁₀ cell kill if the clonogen doubling time is:			Relative late damage ($\alpha/\beta = 3$ Gy)
	> 30 days	7 days	3 days	
Standard				
30F $\times$ 2 Gy = 60 Gy/39 days	9.4	7.7 (18%)	5.5 (44%)	1.00
Strong standard				
35F $\times$ 2 Gy = 70 Gy/46 days	10.9	9.0 (17%)	6.3 (42%)	1.17
EORTC hyperfractionation				
70F $\times$ 1.15 Gy = 80.5 Gy/46 days	11.7	9.7 (17%)	7.1 (39%)	1.11
Concomitant boost				
30F $\times$ 1.8 Gy + 12F $\times$ 1.5 Gy = 72 Gy/39 days	11.0	9.3 (15%)	7.1 (35%)	1.13
Wang (1988)				
42F $\times$ 1.6 Gy = 67.2 Gy/39 days	9.7	8.1 (16%)	6.1 (37%)	1.03
Manchester				
16F $\times$ 3.375 = 54 Gy/21 days	9.4	8.5 (10%)	7.3 (22%)	1.15
Saunders et al (1988)				
36F $\times$ 1.5 Gy = 54 Gy/12 days	8.1	7.6 (6%)	6.9 (15%)	0.81

Assumptions: $\alpha = 0.3 \text{ Gy}^{-1}$; $\beta = 0.03 \text{ Gy}^{-2}$; constant proliferation throughout. Figures in parentheses represent % of full effect lost due to proliferation.

Table VI. List of radiotherapy schedules ranked in decreasing order of "hotness" of late effects in the first column, assuming $\alpha/\beta = 3$ Gy; second and third columns, assuming $\alpha/\beta = 2$ Gy and 4 Gy; note different ranking

Radiotherapy schedule	Late effects (compared with 30F $\times$ 2 Gy as 100%)		
	$\alpha/\beta = 3$ Gy	2 Gy	4 Gy
Strong standard 35F $\times$ 2 Gy = 70 Gy	116.7	116.7	116.7
Manchester 16F $\times$ 3.38 = 54 Gy	114.8	120.9	110.6
RTOG hyperfractionation 68F $\times$ 1.2 = 81.6 Gy	114.2	108.8	117.9
Concomitant boost 72 Gy	113.4	111.8	114.5
EORTC hyperfractionation 70F $\times$ 1.15 = 80.5 Gy	111.4	105.7	115.2
Pipard SAI 70 Gy	111.1	109.7	112.0
EORTC accelerated hyperfractionation 45F $\times$ 1.6 = 72 Gy ^a	110.4	107.5	112.0
Standard 33F $\times$ 2 Gy = 66 Gy	110.0	110.0	110.0
RTOG hyperfractionation 65F $\times$ 1.2 = 78 Gy	109.2	104.0	112.7
Scotland 20F $\times$ 2.8 = 56 Gy	108.3	112.0	105.8
Wang 42F $\times$ 1.6 = 67.2 ^a	103.4	100.8	104.5
Standard 30F $\times$ 2 Gy = 60 Gy	100.0	100.0	100.0
CHART 36F $\times$ 1.56 = 56 Gy	85.0	83.0	86.4
CHART 36F $\times$ 1.5 = 54 Gy	81.0	78.8	82.5

^a4-h intervals. Late effects could be 6 to 9% stronger than listed.

Concomitant boost: 30F $\times$ 1.8 Gy + 12F $\times$ 1.5 Gy = 72 Gy/39 days.

Pipard Swiss Accelerated Irradiation: 10F $\times$ 2 Gy + 30F $\times$ 1.67 Gy = 70 Gy/32 days.

course the same amount of log cell kill would be lost during chemotherapy or any other treatment technique, but it might be a different proportion of the cell killing by the treatment. Table V illustrates this. The difference between the first column (assuming no proliferation) and the others gives the log cell kill which is counteracted by proliferation, with the assumptions shown in the table. If proliferation did not begin until 21 days, the loss in a 6-week schedule would be about half of that shown in Table V. However, for the two treatments listed at the end, which do not exceed 21 days overall time, there would be no loss.

Total dose in a new fractionation schedule

For this application we do not want the overall time factor because late effects will be the dose-limiting consideration. When there is simply a change of dose-per-fraction from a well known schedule ($n_1 \times d_1$) to a new one ($n_2 \times d_2$) the estimate of the new total dose is particularly simple. For equal effects the two values of E or E/α are of course equal:

$$n_1 d_1 (1 + d_1/(\alpha/\beta)) = n_2 d_2 (1 + d_2/(\alpha/\beta))$$

Therefore

$$\frac{n_2 d_2}{n_1 d_1} = \frac{(1 + d_1/(\alpha/\beta))}{(1 + d_2/(\alpha/\beta))} \quad (10)$$

The ratio of total doses is the inverse ratio of the relative effectiveness ($RE = 1 + d/(\alpha/\beta)$).

If the number of fractions is altered instead of the dose-per-fraction, the same equations can be used but the solution of a quadratic is required, as we learned at

school:

$$n_2 d_2 + \frac{n_2 d_2^2}{(\alpha/\beta)} = \text{BED (of the standard schedule)}.$$

Re-arranging this gives:

$$d_2^2 + d_2 (\alpha/\beta) - \text{BED} (\alpha/\beta)/n_2 = 0$$

$$\text{So that } d_2 = -\frac{(\alpha/\beta)}{2} \pm \sqrt{\frac{(\alpha/\beta)^2}{4} + \frac{(\alpha/\beta) \text{ BED}}{n_2}} \quad (11)$$

of which only the positive root is useful. For late effects it is useful to work out several results with different values of α/β , say 2, 3 and 4 Gy as in Table IV.

Comparisons of fractionated schedules

Table VI lists the late effects calculated for some of the currently interesting fractionation schedules. For these, no overall time correction is necessary. It can be seen that the sequence from "hottest" to "coolest" alters a little when different values of α/β are used in the calculation, by up to 5 or 6% of effective damage (BED). Values of 3 Gy are often taken as applying to generalized late connective tissue damage such as fibrosis, ulceration or necrosis. Values for α/β of 1.5 to 2 Gy would apply to spinal cord or brain, 2–3 Gy for kidney and 3–5 Gy for lung.

In order to compare the effects on tumours of the various schedules, the LQ formula with the time factor added can be used (Equation 9). A set of such comparisons is shown in Figs 3–7. These illustrate the principles that have been discussed.

Figure 3 shows the calculated log cell kill, including

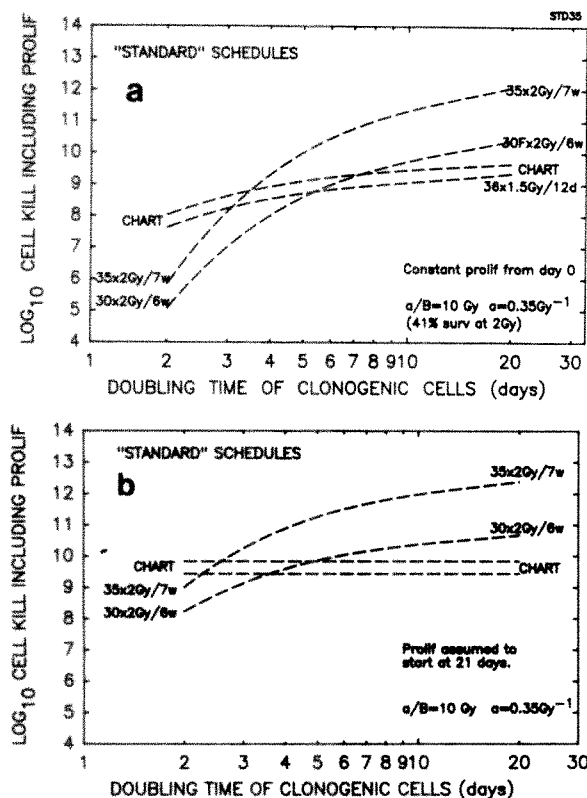


Figure 3. Calculated log cell kill as a function of assumed doubling times of tumorigenic cells from 2 to 20 days for two standard schedules and two dose levels of the continuous hyperfractionated accelerated radiation therapy schedule, totalling 54 and 56 Gy, respectively, in 36F in 12 days. (a) Assuming constant proliferation from Day 0 and (b) assuming that the constant proliferation does not begin until Day 21.

proliferation in the tumour, for two "standard" schedules ($30F \times 2 \text{ Gy} = 60 \text{ Gy}$ in 6 weeks and $35F \times 2 \text{ Gy} = 70 \text{ Gy}$ in 7 weeks) and two dose levels for the highly accelerated continuous hyperfractionated accelerated radiation therapy (CHART) schedule consisting of $36 \times 1.5 \text{ Gy} = 54 \text{ Gy}$ in 12 days, given three times a day with 6-h intervals, including through the weekend (Saunders et al, 1988). This is the most extremely logical extension of accelerated hyperfractionation yet attempted. It is at the opposite pole of current schedules from the 35 fractions of 2 Gy given daily over 7 weeks. Figure 3a is for constant proliferation from the beginning and Fig. 3b is for proliferation assumed to start on Day 21; α is assumed to be 0.35 log_e per Gy. The highest curves in the diagram represent the best tumour control; we do not know for certain whether tumour control would occur between 10^8 and 10^{10} log cell kill or at other levels. One log would lead to a difference of 10 to 15% in local control (Fowler, 1986).

It can be seen in Fig. 3a that proliferation causes a

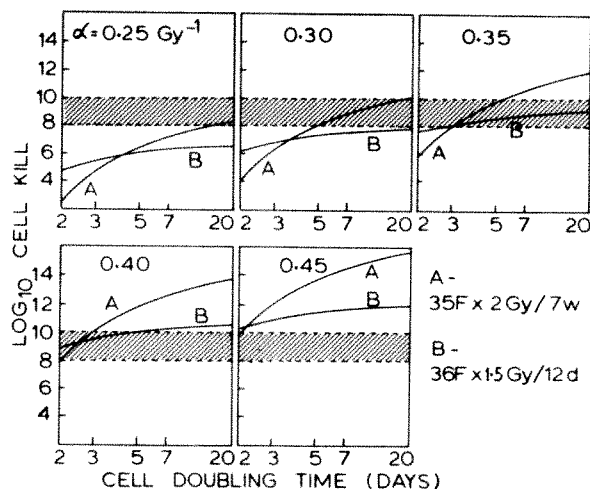


Figure 4. Effect on two of the curves in Fig. 3 of assuming a range of values of α . As the radiosensitivity increases (α increases), the gain from the avoidance of proliferation in the short schedule becomes less important.

rapidly increasing loss of cell kill if the doubling times are shorter than 3 or 4 days. Figure 3a shows that the 7-week schedule loses 6 logs of cell kill, i.e. about half its total effect, if tumour cells proliferate as fast as 2 days doubling time, instead of 20 days. Continuous hyperfractionated accelerated radiation therapy is better than $30F \times 2 \text{ Gy}$ in 6 weeks (in these calculations) for doubling times shorter than 6 or 7 days if proliferation occurs throughout (Fig. 3a) and shorter than 4 or 5 days if proliferation begins at 21 days (Fig. 3b). About half of most types of tumour appear to proliferate as fast as this (Wilson et al, 1988). For the stronger standard of $35F \times 2 \text{ Gy}$, the break-even doubling times are 3–4 and 2–3 days, respectively. Only a minority of tumours would be expected to proliferate as fast as that, unless proliferation becomes even faster during treatment than the pre-treatment values of T_{pot} measured by flow cytometry.

Figure 4 illustrates the effect of intrinsic radiosensitivity and proliferation, by varying the values of α (and β since $\alpha/\beta = 10 \text{ Gy}$ throughout). The log cell kill profiles for the two opposing types of schedule in Fig. 3 are shown: $35F \times 2 \text{ Gy}$ in 7 weeks and $36F \times 1.5 \text{ Gy}$ in 12 days. Results are shown for five values of α ranging from 0.25 to 0.45 log_e per Gy. The major effect is that both schedules pass from total failure, below the arbitrary shaded level of log cell kill for tumour control, to total success above it. However, we are concerned with relative, not actual, cell kill in these comparisons. The break-even doubling time changes from 4.2 to 2.2 days as the tumour cells become more radiosensitive. This means that accelerated fractionation is more worthwhile for radioresistant than radiosensitive tumours, if proliferation rates are equal.

Figure 5 shows the same four curves in Fig. 3 as dashed lines, together with three schedules used in the

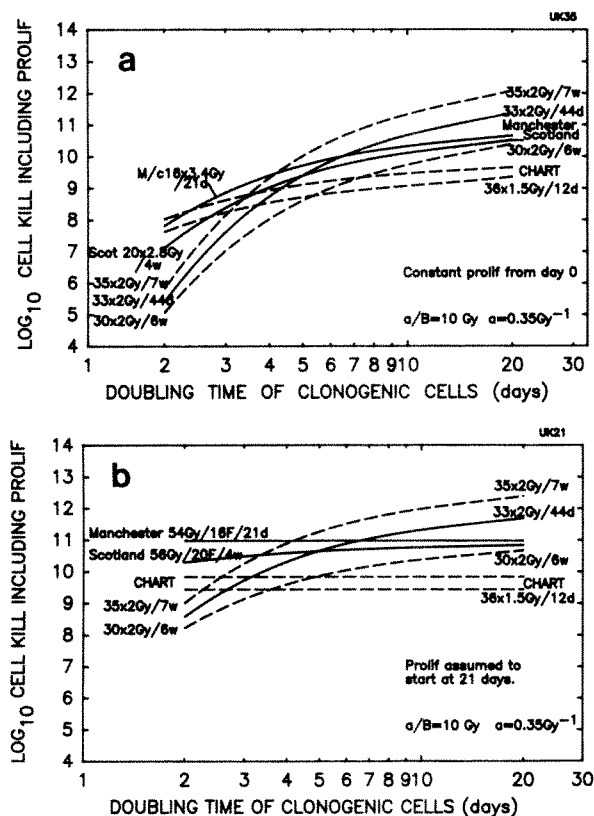


Figure 5. As in Fig. 3: the same four dashed curves are reproduced here, together with solid curves representing three schedules used in the UK as designated. (a) Proliferation assumed constant throughout and (b) proliferation assumed beginning on Day 21.

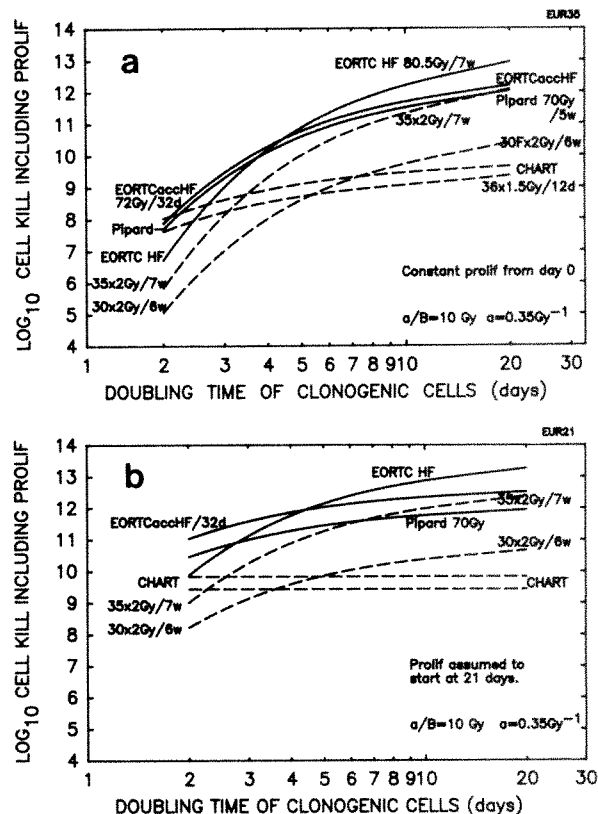


Figure 6. As in Fig. 5, but the three full curves represent three recent European schedules employing hyperfractionation. The EORTC Accelerated Hyperfractionation and the Pipard Swiss Accelerated Irradiation trials also accelerate their treatments to an overall time of 5 instead of 7 weeks.

UK as solid lines. Reading downwards on the right-hand side these are $33\text{F} \times 2\text{ Gy}$ given "daily" = 66 Gy in 6½ weeks, the Manchester schedule of $16\text{F} \times 3.375\text{ Gy} = 54\text{ Gy}$ in 21 days and the Scottish and Canadian schedule of $20\text{F} \times 2.8\text{ Gy} = 56\text{ Gy}$ in 4 weeks. It can be seen that the Manchester schedule is a good competitor with all the schedules except $35\text{F} \times 2\text{ Gy}$. However, its late-damage score is rather high (see Table VI) so its therapeutic gain relative to 30 or $33 \times 2\text{ Gy}$ is probably not very different.

Figure 6 shows similar profiles for three recently designed European protocols (full lines). The completed EORTC hyperfractionation trial ($70\text{F} \times 1.15\text{ Gy}$ given twice daily to 80.5 Gy in 7 Weeks) from which good results have been reported (Horiot et al, 1988) shows an improvement of about 1 log over its own control arm of $35\text{F} \times 2\text{ Gy}$ in 7 weeks. Next is shown the newer EORTC accelerated hyperfractionation trial consisting of three fractions per day of 1.6 Gy to a total of 72 Gy in 5 weeks, with a gap planned after only 28.8 Gy (6 treatment days, 8 real days). This gap is inserted before half of the treatment has been given so that the acute

reactions are less severe and the gap can be less than 2 weeks. Since this schedule employs daytime intervals of only 4 h, it can be calculated (Thames & Hendry, 1987, p. 234) that the early effects, on both tumour and normal tissues, would be 3% hotter, and the late effects 8% hotter, than as shown in Fig. 6 and Table VI, respectively, assuming a half-time for repair of 1.5 h (if repair is faster the excess would be less). The third schedule shown is the Pipard Swiss Accelerated Irradiation which gives an initial boost (to a small volume) of $10\text{F} \times 2\text{ Gy}$ in 2 weeks, followed with no split by $30\text{F} \times 1.667\text{ Gy}$ given twice daily to the full volume, to a total dose of 70 Gy in 5 weeks (Pipard et al, 1988). The latter two protocols were designed to shorten overall times from 6 or 7 weeks to 5 weeks whilst still maintaining a high total dose of at least 70 Gy. They are the shortest high-dose schedules yet planned. Their late effects are not calculated to be excessive (Table VI) except for the possible effects of short fraction intervals, as just mentioned. Here the 8% excess might in fact be critical.

Figure 7 shows similar computed profiles for three of

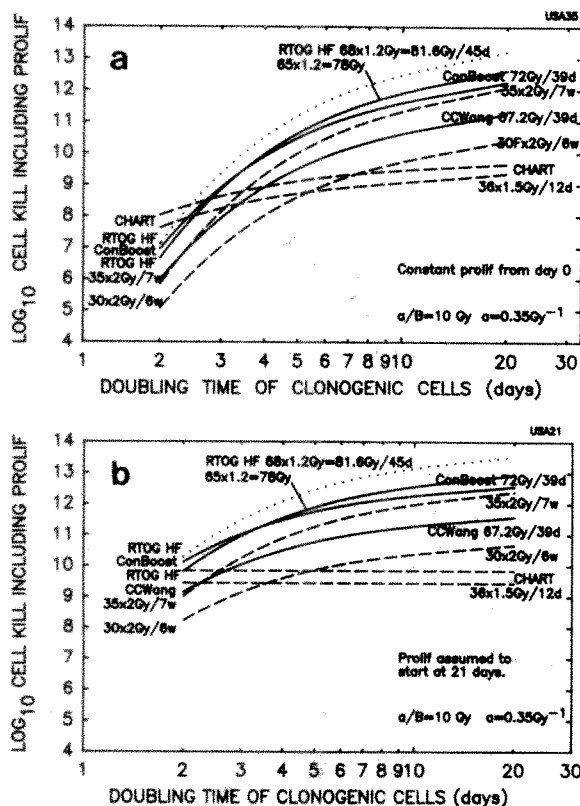


Figure 7. As in Figs 5 and 6, but the three full curves represent three current schedules used in the USA (see text).

the currently interesting USA schedules (full curves) together with a higher escalation of the RTOG hyperfractionated schedule of 1.2 Gy twice daily (shown dotted, uppermost curve: $68F \times 1.2 \text{ Gy} = 81.6 \text{ Gy}$ in 7 weeks). It was from a somewhat lower level of escalation that good clinical results have been reported: $65F \times 1.2 \text{ Gy} = 78 \text{ Gy}$ in $6\frac{1}{2}$ weeks (Parsons et al, 1988). Next down in Fig. 7 comes the concomitant boost schedule designed in Houston, where $30F \times 1.8 \text{ Gy}$ is given in 6 weeks, plus a second treatment on some of the same days in the second half, giving 10 or $12F \times 1.5 \text{ Gy}$ to a smaller "boost" volume without exceeding the 6-week overall time (Knee et al, 1985). The total dose is 69–72 Gy in 39 days. The third schedule is that of Wang (1988) who gives 1.6 Gy fractions twice daily to a total of 67.2 Gy in 6 weeks, with a gap of 2 weeks after 38.4 Gy in 12 treatment days, 2½ weeks.

Intervals between fractions

Because the daytime interval was only 4 h, it would be expected that the early tumour effects in the Wang and Parsons schedules would be 2% hotter and late effects 6% hotter than shown in Fig. 7 and Table VI, respectively, assuming a half-time of repair of 1.5 h.

Table VII list the correction factors for fraction intervals when 2F or 3F per day are given, for several

Table VII. Per cent extra effective dose for interfraction intervals of 4, 6 and 8 hours

Schedule (and half-time of repair)	Late effects			Early and tumour effects		
	4 h	6 h	8 h	4 h	6 h	8 h
2 fractions/day						
2 × 2 Gy						
(2 h)	10.0	5.0	2.5	4.2	2.1	1.0
(1.5 h)	6.3	2.5	1.0	2.6	1.0	0.4
2 × 1.6 Gy						
(2 h)	8.7	4.4	2.2	3.5	1.0	0.9
(1.5 h)	5.5	2.2	0.9	2.2	0.9	0.3
2 × 1.2 Gy						
(2 h)	7.1	3.6	1.8	2.7	1.3	0.7
(1.5 h)	4.5	1.8	0.7	1.7	0.7	0.3
3 fractions/day						
3 × 1.6 Gy						
(2 h)	13.0	6.5	3.3	5.2	2.6	1.3
(1.5 h)	8.2	3.3	1.3	3.3	1.3	0.5
3 × 1.2 Gy						
(2 h)	10.7	5.4	2.7	4.0	2.0	1.0
(1.5 h)	6.8	2.7	1.1	2.5	1.0	0.4
3 × 1.0 Gy						
(2 h)	9.4	4.7	2.3	3.4	1.7	0.9
(1.5 h)	5.9	2.3	0.9	2.2	0.9	0.3

fraction sizes but only two assumed half-times of repair. These corrections should be applied to the Gy_3 (late) or Gy_{10} (tumour and early) biologically effective doses. Figure 8 shows the corrections for a wider range of fraction sizes and intervals.

General strategy for optimum fractionation

Withers (1988) has summed up the strategy of fractionated radiotherapy succinctly: Give as high a dose as you can give without causing severe late effects, using smaller doses per fraction than 1.8–2 Gy to keep the late effects moderate compared with tumour cell kill; and give this dose in as short an overall time as you can without causing severe acute effects. Clinical experience has shown that $3F \times 2 \text{ Gy}$ per day cannot be given without causing severe acute effects. The maximum dose per day that can be given, whatever the fractionation, appears to be no more than 4.8 or 5 Gy (except for very low dose-rates).

Multiple fractions per day are an essential feature of all the recently designed, radiobiologically based, high-performance schedules, whether hyperfractionated, accelerated or both (Thames et al, 1989).

No more than about 55 Gy can be given within 2 weeks by any schedule, or acute effects became too severe. Whether this modest dose can compete with 70 Gy or so in 5–6 weeks depends on the proliferation rates of tumour cells. A substantial proportion of tumours may be better treated by these very short schedules, but by no means all tumours, as illustrated in Figs 3–7. It is known that good clinical results can be obtained with schedules as long as 6 or 7 weeks. The

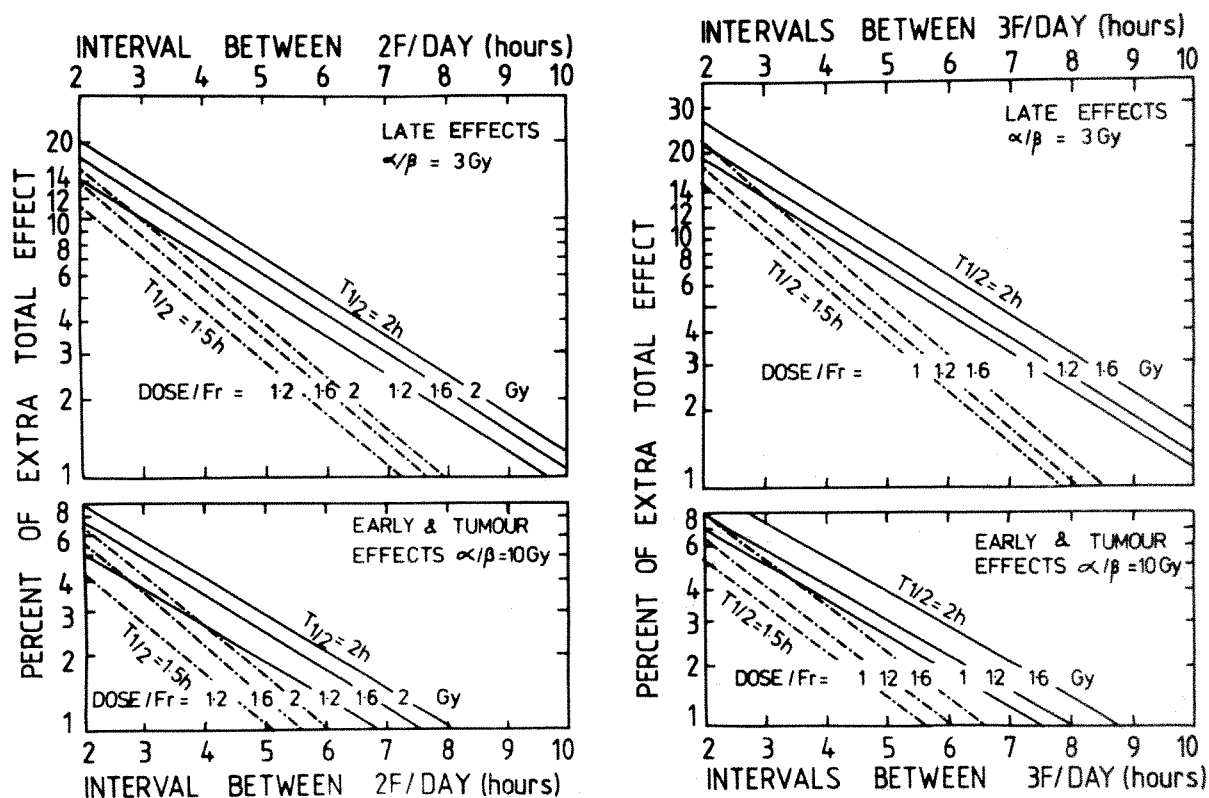


Figure 8. Excess proportion of effect (BED) caused by using daytime intervals as specified between either 2F/day or 3F/day.

question is whether the failures are due to very rapid proliferation.

The high-dose, accelerated, hyperfractionation schedules delivering about 70 Gy in 5 weeks, as employed in Europe, appear at present more likely to be generally effective than the ultrashort schedules with their limited total doses, unless there is even faster proliferation induced during the treatment than is measured by flow cytometry from biopsies taken before treatment. If so, the results of the CHART trials will come out even better than expected. This is one of the major biological questions to tackle in human tumours. We cannot yet interpret cell kinetic measurements made in tumours during non-equilibrium conditions, *i.e.* during treatment. It is a challenge to find ways of doing this.

The LQ model, with the addition of the proliferation time factor, becomes more clumsy and dangerous than the simple LQ model used (correctly without a time factor) to calculate for late effects. But it focuses attention on the important biological parameters, as good models should. We need to continue to develop ways of measuring intrinsic radioresistance and proliferation rates *during* treatment.

The ideal situation will be to use the assay methods that are now being tested to allocate patients to different types of treatment schedule, based on individual

measurements of their tumour cell radiosensitivity and proliferation rate. There is now some hope that we are approaching that situation.

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Screening for breast cancer: the UK scene

The 69th Mackenzie Davidson Memorial Lecture*

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Sir James McKenzie Davidson was born in 1856, 39 years before Röntgen discovered X rays. A graduate of the University of Aberdeen, his initial training was in surgery (and what better for a future radiologist!) and ophthalmology. It was following a visit to Wurzberg that he decided to devote his energies to the new specialty of radiology and was appointed to Charing Cross and the Royal London Ophthalmic Hospitals. There he was instrumental in pioneering many new developments, including the use of stereoscopy for localizing foreign bodies, a method of great benefit to the wounded of World War I.

McKenzie Davidson continued to pioneer new developments up to his untimely death at the age of 63 years (Obituary, 1919; Burrows, 1986). Thirty of his colleagues, including Prime Minister Stanley Baldwin, set up a memorial fund, which was used to help purchase 32 Welbeck Street as a home for the Röntgen Society or, as it became in 1924, your British Institute of Radiology. Furthermore, his widow and family endowed this Memorial Lecture so that his name could be kept alive in radiological circles. And so it should be, for McKenzie Davidson was not only a pioneer and innovator but, from all accounts, a warm and generous man, bringing distinction to the field in which he was truly a founding father. It is a great honour to be invited to deliver this lecture in his memory.

It was in 1987, 90 years after McKenzie Davidson commenced his career in radiology, that it was decided to use radiology to reduce the appalling mortality in UK from breast cancer, and institute a national programme of mammographic screening of normal women. To understand why its mortality has not changed, one must be aware of the history surrounding the management of the disease since the time of McKenzie Davidson's youth. It was in 1867 that the first "radical" operation for breast cancer, removing not only the breast but the axillary lymph nodes, is believed to have been performed, this by Professor Lister in his home in 17 Woodside Place in this city of Glasgow. As previous attempts at other than the simplest of surgery for breast cancer were fraught with danger of infection and death, the operation was "new and dangerous" for it was only 2 years since Lister's introduction of the

antiseptic treatment of a compound fracture and only 2 months since this was first applied to a surgical wound (Godlee, 1917; Logan Turner, 1927). Furthermore, the patient, Isabella Pim, was his sister, who before consulting her brother, had been seen by James Paget in London and James Syme in Edinburgh who considered her disease too advanced for surgery. No wonder that Lister described the operation as a "formidable undertaking". Nevertheless, she made an uneventful recovery and lived for 3 years before succumbing to metastatic disease.

Lister took his operation with him to Edinburgh, where he occupied the Regius Chair of Clinical Surgery when McKenzie Davidson was a schoolboy. Following a visit by Volkmann to Edinburgh, the operation came to be practised in Europe, where it was extended by partial or complete removal of the underlying pectoral muscles; following a visit by Halsted to Europe, it spread to North America where it was finally perfected (Halsted, 1894, 1907). The Halsted radical mastectomy became the "gold standard" for the management of breast cancer throughout the surgical world.

The prime purpose of this radical operation was to improve local control and reduce the high local and regional recurrence rates that then followed local treatment. However, false beliefs were brought to bear, suggesting that it might also cure the disease. It was mainly as a result of the teachings of Sampson Handley (1906) that cancer of the breast was regarded as a regional disease, which spread predominantly by the slow permeation of tumour along regional lymphatic channels. As embolized cells were believed to be filtered out by the axillary lymph nodes (Virchow, 1863), they posed little hazard: involvement of bones and viscera was considered a late and delayed phenomenon. Furthermore, Halsted had suggested that survival of the patient without recurrence for 3 years after treatment was indicative of cure (Halsted, 1907). It was this concept of the disease that led to the erroneous view that the more extensive the local treatment, the more likely was cure to be achieved; this ushered in more radical surgery and the addition to radical surgery of radical radiation therapy.

It has taken almost a century to dispel these beliefs, awaiting new evidence that the spread of cancer was primarily an embolic phenomenon (Cole, 1961; Fisher & Fisher, 1966) and that wide dissemination of malignant cells occurred early in its natural history. Furthermore,

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reports of controlled randomized trials have indicated that neither extension of surgery nor the addition of radiotherapy reduced the mortality of the disease (Lecour et al, 1983; Cuzick et al, 1987). Even more significant are the results of several long-term follow-up studies indicating that, following standard local therapy, progressive and relentless death from metastatic disease occurs in most patients, continuing for even 30 years after primary treatment (Fig. 1) (Brinkley & Haybittle, 1984). Invasive breast cancer is now regarded as a systemic, not a regional, disease and one that is incurable by local means alone. Early dissemination with the subsequent growth of micrometastases determines its potential for a fatal outcome.

It is as a result of this knowledge that measures have been developed that now have an impact on its mortality: first, the addition to primary local surgery and radiotherapy of systemic treatment (by hormonal agents or chemotherapy) to eliminate or retard the growth of micrometastatic disease (Early Breast Cancer Trialists Co-operative Group, 1988) and secondly, the detection of the disease before it has disseminated and therefore is at a stage when it can be cured by local treatment alone. It is the second of these measures that forms the basis of this lecture.

Natural history

Three of the principles that require to be met before mass population screening can be justifiably introduced (Wilson & Jungner, 1968) are that the natural history of the disease should be understood, that there is a recognizable early stage and that there should be a sensitive and reproducible method to detect it.

Breast cancer is a disease affecting the epithelium of the secreting units of the breast, the "terminal duct-lobular units" (Fig. 2), which consist of terminal ductules and acini encased in fine connective tissue and surrounded by fat. These functional units are under hormonal control; well developed lobules appear to be necessary for the development of breast cancer (Wellings et al, 1975).

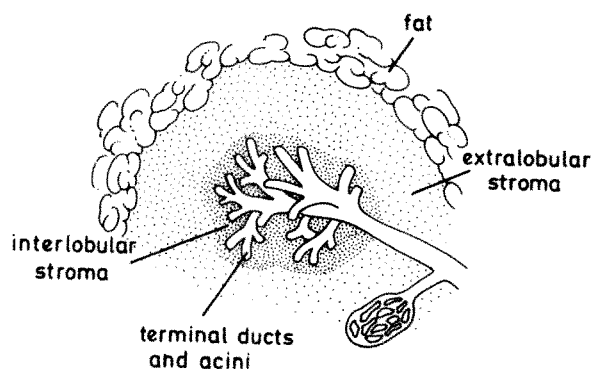


Figure 2. Terminal duct lobular unit of the breast: the secreting gland.

A series of changes affecting the epithelium of the secreting units are believed to precede cancer (Wellings et al, 1975; Page & Anderson, 1987). Earliest is an increase in the number of cells (hyperplasia), which, if excessive and of abnormal pattern, becomes "atypical". Frank features of malignancy in the cells lead to the formation of *in situ* (non-invasive) cancer; the next stage is that of invasion. These changes do not always progress but may be self-limiting at any stage. However, they are not uncommon.

In situ cancer is by definition non-invasive and curable by local treatment alone. The occasional occurrence of lymph-node metastases is probably due to undetected foci of microinvasion. Invasive cancer is potentially incurable, but it appears that there is a threshold of size at which it is more likely to have metastasized. The initial studies of Gallagher and Martin (1971) suggested that this was 0.5 cm or less. Collating data from four centres (Table I), Gallagher has reported recently that invasive tumours of this size have a low incidence of axillary node metastases and an uncommonly good prognosis (Gallagher, 1983). The Breast Cancer Detection Demonstration Project has put this threshold higher (1.0 cm) and this has gained worldwide acceptance (Working Group, 1979; Seideman et al, 1987). However, it is more likely that there is a gradient between size, metastatic potential and prognosis.

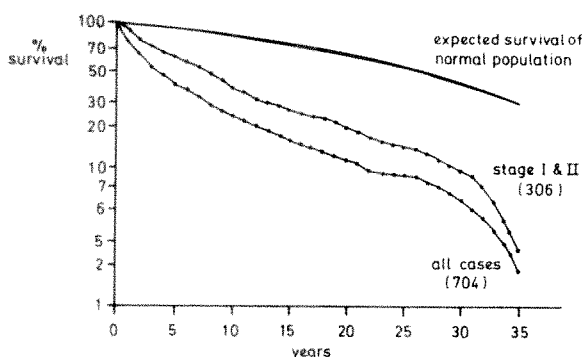


Figure 1. Long-term survival of 704 patients with breast cancer treated in East Anglia between 1947 and 1950 (from Brinkley & Haybittle, 1984).

Table I. Axillary node involvement rates in 415 patients and relapse-free survival in 411 patients with "minimal" breast cancer

	Axillary node involvement	Alive with no evidence of recurrence 1-26 years
Non-invasive	2-4%	—
Invasive <0.5 cm	13%	—
Total	5.5%	96.8%

Taken from Gallagher (1983).

In situ and small invasive cancers have been termed "minimal" disease. It is the objective of screening to detect cancer at this stage. Modern mammography, using dedicated equipment and film-screen combinations, can do so.

Proof of benefit

Another principle that requires to be met before mass-population screening can be introduced is that it should be of proven benefit. For breast cancer, proof rests on the demonstration in two randomized controlled studies involving over 200 000 women, carried out in the United States and in Sweden (Shapiro et al, 1982; Tabar et al, 1985; Venet & Shapiro, 1986), of a reduction in mortality from the disease in those invited to participate in screening.

In one trial, conducted by the Health Insurance Plan of Greater New York (HIP study), 62 000 women aged 40–64 years were randomly allocated either to be offered screening by two-view mammography and clinical examination at entry and annually for three further occasions, or to receive only their normal medical care. Ten years following entry to the trial there were 30% fewer deaths from breast cancer (diagnosed within 7 years of entry) in the study group than amongst their controls, an effect that has persisted in lesser degree for 18 years (Table II).

The Swedish trial involved 63 000 women over 40 years of age living in two counties (WE study) who were also randomized to be invited to be screened on two occasions by single medio-lateral oblique mammography or to receive their normal medical care. The frequency of screening was, on average, 24 months for those under 50 years and 33 months for those 50 years and more. Over 8 years, breast cancer mortality has been reduced by 31% in those invited to be screened (Tabar et al, 1987). In both these studies, a significant effect has been observed only in women over the age of 50 years.

The reduction in mortality reported in these two randomized trials has been supported by three case-control studies in the cities of Nijmegen, Utrecht and Florence, where regular mammographic (and, in some, clinical) screening was introduced during the 1970s (Collette et al, 1984; Verbeek et al, 1984; Palli et al, 1986). A comparison of the screening history of those women who died from breast cancer diagnosed since screening with that of age-matched living controls free

from the disease is compatible, with a reduction in breast cancer deaths in screened women of approximately 50%.

Pattern of screen-detected cancer

Following the introduction of regular mammographic screening (with or without clinical examination of the breasts), the pattern of breast cancer changes. Compared with symptomatic cancers, those detected through screening are more likely to be non-invasive and, if invasive, to be smaller, more commonly of special histological type and less commonly associated with axillary node involvement. Furthermore, their survival rates are significantly prolonged. These findings are not free from bias. Screen-detected cancers are more likely to be diagnosed early in their natural history (lead-time bias), to be slower growing (length bias) and to occur in health-aware women (selection bias). However, as this pattern is associated with subsequent reduction in mortality, it can be used to monitor the likely success of a screening programme in its early years. Recent results from the large Breast Cancer Detection Demonstration Project, involving some 280 000 women in the United States, demonstrate this pattern of change (Table III) (Seideman et al, 1987).

UK trials

In 1979, a study was set up in the UK (Trial of Early Detection of Breast Cancer (TEDBC)) involving some 300 000 women aged 45–64 years living in eight health authority districts (UK TEDBC, 1981). In two centres (Edinburgh and Guildford), women were invited to be screened annually on seven occasions by clinical examination, with mammography at Years 1, 3, 5 and 7. In two centres (Huddersfield and Nottingham), women were invited to participate in instruction in self-examination of the breasts (BSE) backed up by a self-referral clinic offering full investigation of suspected abnormalities. In the remaining four comparison districts (Dundee, Oxford, Southmead and Stoke), women received only their usual medical care. A first analysis of mortality will be available in a few months.

The Edinburgh contribution to the national study was

Table II. Deaths from breast cancer (diagnosed within 5 years of entry) in the population invited to be screened and their controls

	5 years	10 years	18 years
Study	39	95	126
Control	63	133	163
% reduction	38.1%	28.6%	22.7%

Taken from Venet & Shapiro (1986).

Table III. Characteristics of "minimal" cancers in the BCDDP project

Total number	1153
Non-invasive	782
<1.0 cm invasive	371
Axillary node involvement	758 cases
Non-invasive	3.4%
<1.0 cm invasive	16.5%
Overall	9.0%
Recurrence-free survival at 10 years	893 cases
Non-invasive	96%
<1.0 cm invasive	81%

extended by the institution of a controlled randomized trial. In this, 70 000 women were randomly allocated in batches, determined by the general practice with which they were registered, either to be invited to be screened (as in the national programme) or as controls (Roberts et al, 1984). Although case survival and mortality statistics are not yet available, it is apparent that, compared with women in the control population, women who have attended for screening have a greater proportion of non-invasive cancers, invasive cancers that are smaller, cancers that are more likely to be of special histological type and with a lower incidence of axillary node involvement (Anderson, T. J., 1988, personal communication) (Table IV). This is the pattern observed in other studies and associated with a reduction in mortality. As social class is known to affect mortality from breast cancer as well as the response to an invitation to be screened (French et al, 1982), neither one of these British studies can be regarded as completely free of bias.

The national screening programme—basic screen

Conviction that the early detection of breast cancer was of proven benefit has led to the implementation of a national programme of screening in the UK. Women aged 50–64 years are being invited to either static or mobile mammographic screening units for medio-lateral oblique mammography of both breasts every 3 years. The recommendations on which the programme is based are initial ones and may need to be modified in light of further information (HMSO, 1987).

Single-view mammography

The decision to advocate single medio-lateral oblique-view mammography of each breast as the basic screening procedure was based on Swedish experience. Introduced by Lundgren as the most suitable view to include most breast tissue, it has now largely replaced the lateral view in all centres (Lundgren & Helleberg, 1982). Swedish experience has indicated that recall rates are satisfactorily small and that the sensitivity for the detection of cancer (based on interval cancer rates) exceeds 90% (Lundgren, 1979). In Nijmegen, also, single-view mammography was, and remains, the sole method of breast screening.

British radiologists are uncertain that single-view

Table V. Results of a retrospective study of single- versus two-view mammography (the same radiologist reading radiographs twice) in 2500 consecutive asymptomatic women

	Medio-lateral oblique view only	Medio-lateral oblique plus craniocaudal views
Interpreted as abnormal	642	179
Mammographic abnormality generated biopsy	76	83
Generated diagnosis of cancer	25	27

Taken from Sickles et al (1986).

mammography is adequate for basic screening. Evidence from two European studies, in which single oblique mammograms have been retrospectively interpreted alone and then in combination with a cranio-caudal (and, in one study, lateral) view, indicates a “miss-rate” for cancer on the single view of 4% in Sweden but 11% in the UK (Andersson et al, 1978; Muir et al, 1984). North American studies give similar cancer detection rates but, in both, the request rate for mammograms additional to the oblique view is reported to be in the region of 30%, which is unacceptable (Tables IV, V, VI). In Sweden, it approximates 5%, and in Edinburgh and Guildford (where single-view mammography has been used for repeat (incidence) screens, it is 10%. The difference between the North American and European experiences requires explanation.

These studies are retrospective and therefore unsatisfactory as they are not carried out under a “real” situation. There is need for a prospective trial, in which women invited to be screened are randomly allocated either for single- or two-view mammography on each of which a decision must be made by the radiologist. Monitoring should include recall rates, cancer detection rates and interval cancer rates. Such a trial is currently being planned in the UK. In the meantime, single-view mammography remains the advised basic screening method in the UK. Exceptions may be necessary in rural areas where recall for additional mammographic views

Table IV. Characteristics of cancer in study and control groups in the Edinburgh randomized trial

	Total no. of cancers	Non-invasive (%)	<2.0 cm (%)	Axillary node negative (%)
Study population	265	—	—	—
Ffirst (prevalent) screen	—	16.1	76.6	77.3
Incident screen	—	16.3	72.3	59.8
Refused screen	—	4.0	33.4	42.6
Control population	248	2.4	39.5	50.6

Taken from Anderson, 1988, personal communication.

Table VI. Comparison of single- versus two-view mammograms from 169 patients with cancer and 194 healthy controls, read by three radiologists

	Patients with cancer (<i>n</i> = 169)		Normal women (<i>n</i> = 194)	
	Medio-lateral oblique view only	Oblique plus cranio-caudal	Medio-lateral oblique view only	Oblique plus cranio-caudal
Interpreted as abnormal	90%	84%	39%	12%
Recommended additional view	23%	4%	32%	5%
Recommended for biopsy	67%	80%	7%	7%

may pose difficulty, but research is again necessary to determine this.

Some still believe that clinical (physical) examination of the breasts should be a routine part of screening (Hansell et al, 1988). This view disregards improvements in mammographic techniques. In the HIP study, 45% of 132 cancers detected through screening would have been missed had clinical examination not been performed: 10 years later the figure from BCDDP was less than 10% (257 of 3437 cancers) (Shapiro et al, 1982; Seideman et al, 1987). In the Edinburgh project, only 6% of cancers were detected by clinical examination alone. Provided mammography is of high quality, clinical examination is neither necessary nor economically justified, and cannot be recommended as part of screening, at least in women of the age group under test.

Age

The age of the target population to be screened in the UK is 50–64 years. The upper age limit reflects the fall-off in response rate in older women (who, however, may still attend for screening on request). The younger limit was determined by the lack of statistically valid evidence that women under 50 years benefit. In the HIP and WE studies, the observed reduction in mortality is due to the effect of screening in older women. Although with the

passage of time from entry to the programme, some benefit may be appearing in younger women, this is not of statistical significance (Fig. 3). Further evidence will not become available from the HIP study; the final report has now been issued (Venet & Shapiro, 1986).

It is well recognized that mammography is less sensitive in detecting abnormalities in the dense breasts of young women. In the WE study, interval cancer rates within 12 months of screening women of 40–49 years were 38% and between 12 and 24 months were 68% of expected spontaneous incidence rates (Tabar et al, 1987). It is advised in Sweden that, in women of 40–54 years of age, two-view mammography should be used for the basic screening and repeated each 18 months (National Board of Health & Welfare (NBHW, 1986)).

There is a need for further studies and, in Britain, a prospective randomized trial of screening in women aged 40–50 years is under consideration.

Frequency

The recommendation that mammographic screening should be repeated every 3 years was also based on the Swedish WE study. Women of 50 years of age and over attended for repeat screening at an average of 33 months. Mortality reductions were similar to those observed in the HIP study, in which four episodes of

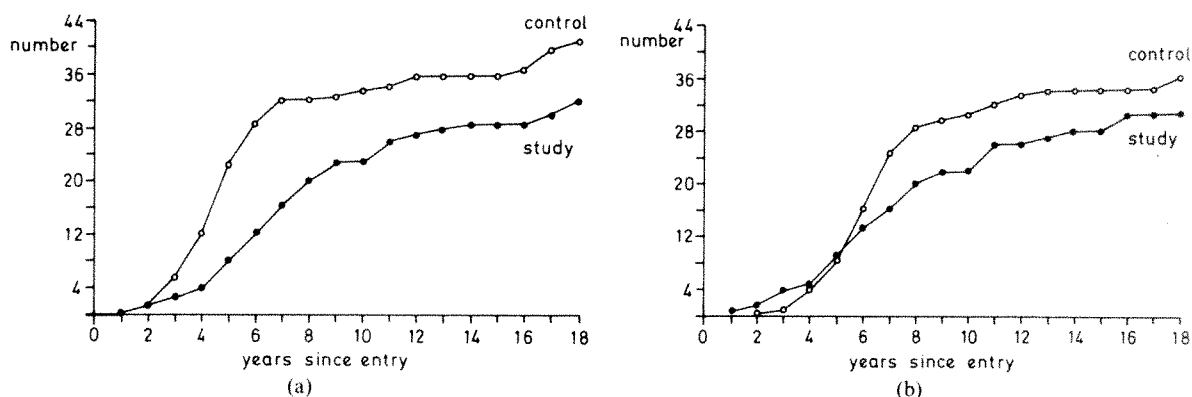


Figure 3. Comparison of mortality from breast cancer in study (invited to be screened) and control groups in HIP study: (a) women of 50–54 years of age and (b) women of 40–49 years of age (from Venet & Shapiro, 1986).

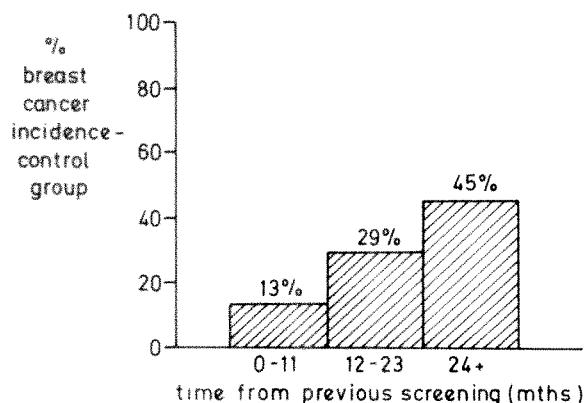


Figure 4. Interval cancer rates in a Swedish, two-counties study expressed as percentage of incidence of breast cancer in the control group: women of 50-69 years of age, screened at an average interval of 33 months (from Tabar et al, 1987).

screening were performed annually. Swedish experience indicates that, in women over 50 years, interval cancer rates climb rapidly between the 2nd and 3rd year following the initial screen, so a shorter interval may be desirable (Fig. 4). A prospective study to examine this question is also being planned in Britain.

The initial recommendations of the Working Group on Breast Cancer Screening may require modification with time. Hard evidence is required and this can only come from well designed and meticulously conducted controlled randomized trials. In the UK, we have a unique opportunity to carry these out, but only after a high-quality service has been established. A sub-committee of the UK Co-ordinating Committee on Cancer Research (Breast Screening Research Sub-committee) has been set up to suggest and co-ordinate such studies.

Assessment

Another principle of screening is that facilities for the diagnosis of screen-detected abnormalities should be available. Mammographic screening is only the first step in the screening process, providing information as to whether there is an abnormality on the mammogram or not. A decision on the significance of this abnormality and whether a biopsy is required depends on the care with which this assessment is carried out. If the quality is poor, not only may there be unnecessary biopsies and unnecessary concern to the woman, but an occasional "blind" mastectomy, which is criminal. The best guide to the quality of the assessment procedure is the number of biopsies performed and the ratio of benign to malignant disease in the excised specimen. In good screening programmes, the proportion biopsied should not exceed 1.5% for the first (prevalent) screen and 1.0% thereafter. In the Swedish WE study, the ratio of benign to malignant biopsy was 3:2 for the first screen and 1:2 for subsequent screens. In Edinburgh, these ratios were 2.7:1 and 1.8:1, respectively. In the large

BCDDP study in the United States, not only were the number of biopsies in excess of that in European centres but the ratio of benign to malignant biopsies was 5.7:1 for the prevalent and between 4.0 and 6.0:1 for subsequent screens (Seidman et al, 1987). In the United States, many believe that all mammographic lesions should be removed—this is quite without justification and reflects inadequate evaluation of the significance of mammographic abnormalities.

The methods available for assessment include clinical examination, additional mammographic views, magnification mammography, ultrasonography, fine-needle aspiration (to differentiate solid from cystic lesions) and fine-needle aspiration cytology (to provide a cytological diagnosis of a solid lesion).

Clinical examination is required for all patients reporting symptoms at their basic screening examination. If practical, a physical examination is probably also advisable for all women with a mammographic abnormality unless this is of such minor importance that the radiologist feels a cranio-caudal view is sufficient further investigation. An initial clinical examination can be delegated to a clinic doctor, but some surgeons would wish to be involved at this stage. Experience in Edinburgh and Guildford suggests that if single-view oblique mammography is used for the basic screen, some 10% of women will require a second view. It is at this stage that the radiologist may also wish for a magnification view to define the type and number of calcifications, the border of a small opacity or the underlying cause of an architectural abnormality. He may also wish to perform ultrasonography to differentiate the small, solid lesion from the cystic lesion, although if a mass is palpable, fine-needle aspiration is both simpler and more effective.

If cancer cannot be ruled out, further assessment is required. This is more complex, requiring the resources of a multi-disciplinary team consisting of radiologist, surgeon and cytopathologist, all experienced in the problems associated with the diagnosis of screen-detected lesions. It is at this stage that invasive techniques such as fine-needle aspiration will be necessary but, before this is performed, the surgeon responsible for the biopsy must have an opportunity to examine the lesion clinically. Otherwise the reaction caused by the needle puncture may confuse its characteristics or give a false impression of size.

If the mass is palpable (and in Edinburgh 70% of screen-detected abnormalities proved to be so), fine-needle aspiration with (if indicated) cytology are relatively straightforward investigations. The situation is no different from that in symptomatic patients in whom the establishment of an accurate pre-operative diagnosis is now the rule in all specialized centres. Fine-needle aspiration of an impalpable mass is possible only with ultrasound (if cystic) or radiological (if solid) guidance. The latter requires stereoscopic control, using the same principle that McKenzie Davidson described in 1912.

Various devices have been developed, that of

Table VII. Malmö experience of 167 solid non-palpable mammographic lesions (an additional 48 (22%) were cystic)

Report of cytology ^a	Total	Final diagnosis on grounds of clinical (70) and histopathological finding (97)	
		Malignant	Benign
Failed	30	8	22
Malignant	34	33	(1 no operation)
Atypia indicating surgery	8	3	5
Atypia — slight	9	1	8
Benign	86	2	84
Total	167	47	120

^aStereotaxic aspiration cytology. Taken from Lofgren et al (1988).

Nordstrom being the most sophisticated (Bolmgren et al, 1977). This uses a computerized "plotter", which allows the needle to be directed to the lesion under remote control. Recent reports from Malmö (Lofgren et al, 1988) and Nijmegen (Hendricks, 1988, personal communication) indicate the diagnostic value of this technique (Table VII).

In Edinburgh, Dent and his colleagues explored its use in 50 consecutive patients with impalpable mammographic lesions, all of which were subsequently removed for histopathological examination (Dent et al, 1989). A satisfactory specimen for cytology was obtained in only 85% of cases, but this was their initial experience. As with all cytological techniques, a positive diagnosis of malignancy cannot be disregarded but false negative results can occur (Table VIII).

Two matters regarding assessment must be stressed. First, a logical decision concerning the need for biopsy can only be made when all relevant information from the assessment procedure is available. The opinions of all members of the assessment team must be co-ordinated before advice is given to the patient, otherwise

Table VIII. Stereotactic aspiration cytology: preliminary experience in Edinburgh (Dent et al, 1989)

Report of cytology	Total	Histopathological diagnosis	
		Malignant	Benign
Failed	15	4	11
Malignant	6	6	—
Suspicion of malignancy	6	1	5
Benign	23	2	21
Total	50	13	37

she can only become confused and worried by what may be the different opinions of individual members. In most centres in the UK, a surgeon takes this responsibility and, with a nurse counsellor, interviews the patient following completion of her investigations. Secondly, the quality of the assessment procedure must be beyond reproach. This applies particularly to the radiological assessment, which is critical to future action. Slipshod assessment of mammographic abnormalities and the performance of unnecessary biopsies must not become part of the British scene.

Biopsy

The third stage in the screening process is a surgical biopsy. If a palpable solid mass is present, the diagnosis should have been reached pre-operatively, so that an appropriate operation can be planned. If the lesion is benign (or in occasional cases, too small for accurate needle puncture) it is simple to remove it under local anaesthesia as a day-case.

It is in the management of the impalpable lesion that special skills are required. These are not only surgical but also radiological, so that excessive tissue removal, with distortion of the breast, can be avoided. Precise peroperative localization of the lesion is required and various methods have been described. Initially, these consisted only of skin markers, but it was soon apparent that a radio-opaque and visible marker within the breast tissue was a necessary guide to the surgeon. Our preference is for the Frank hooked stylet, which is inserted by the radiologist immediately before the operation so that its position relevant to the lesion is demonstrated on the radiograph (Frank et al, 1976). Others prefer to inject a solution containing a radiological contrast medium and a visible dye (Simon et al, 1972) but, because of staining of the tissues, this may make the selection of tissue for sectioning more difficult.

We prefer to carry out localization biopsy under general anaesthesia, although in the USA many surgeons use local anaesthesia. The marker is identified and removed with the lesion and a small amount of surrounding breast tissue. Confirmation that the mammographic abnormality has been removed is necessary and requires immediate specimen radiology, most easily performed with a dedicated machine in the operating suite. This investigation is mandatory, and only following such confirmation is the specimen given to the pathologist. Ideally, the radiological member of the assessment team should be present and should take responsibility for interpreting the radiograph.

The histopathological examination of the small screen-detected abnormality cannot be regarded as a "routine" procedure. The pathologist will wish to obtain the specimen unfixed so that it can be sliced, radiographing each slice so that those areas he/she wishes to examine histologically can be identified. In cases of suspected malignancy, the pathologist will also wish to perform an oestrogen-receptor assay, now possible by histochemical means (Hawkins et al, 1989).

There is no place for the immediate examination of the specimen by frozen-section techniques. The interpretation of the small, mammographically detailed lesion requires the skill and time of a pathologist experienced in the diagnosis of these lesions and the implications for treatment.

Treatment

The final stage of the screening procedure is that of treatment, and this demands knowledge of the natural history of the *in situ* (non-invasive) and small invasive cancer. In those with *in situ* disease (and this may be of ductal or lobular type) it is important to know the risk of invasive cancer in one or other breast (Swain & Lippman, 1988), otherwise one cannot discuss with the patient the options for treatment, which extend from simple excision alone to mastectomy. While mastectomy is still considered the only sure treatment by many (and reconstruction of the breast is now readily performed), others have moved towards greater conservatism. There are now several randomized trials in progress in Europe and the US in which local excision alone is being compared with local excision plus radical radiation therapy. A trial is under discussion in the UK.

For the treatment of the small invasive cancer, wide local excision and radical radiation therapy is now considered to be an acceptable alternative to mastectomy (Tobias & Peckham, 1985). In Scotland, we are currently studying the need for radiotherapy in tumours of less than 4 cm in size, provided that the local excision is supported by systemic therapy either with the anti-oestrogen tamoxifen or chemotherapy, this by a randomized controlled trial.

Mastectomy would seem to have little part to play in the management of these small lesions, and this must be counted as a positive benefit of the institution of a screening programme.

Economics

Two final principles of screening to be considered are that cost should not outweigh benefit and that adequate resources should be available, not only for screening but also for the diagnosis and treatment of the screen-detected cancer. In the report of the Working Group, it was indicated that the cost of the proposed UK programme was not excessive compared with other health costs. When calculated in terms of quality adjusted life years (QALYs) the cost was only slightly greater than that of renal transplantation and less than that of medical treatment of mild hypertension or surgery for single-vessel coronary artery disease (HMSO, 1987).

Some are concerned that the load put on the hospital service may be excessive. Recent information from Sweden suggests that, following the introduction of screening, there is a considerable increase in the number of patients requiring treatment for breast cancer but not for benign disease (Holmberg et al, 1986). However, this increased need forms a temporary "hump" and should return to pre-screening levels in 5–7 years.

Table IX. Manpower resources required for the UK Screening Programme

	<i>n</i>
Radiologists	48
Radiographers	204
Clinicians (including surgeons)	24
Nurses	24
Pathologists	12
Administrators and secretaries	558
Technical (dark-room, drivers, etc)	120

Cost is not only financial. The total resources required for a nationwide programme of screening are considerable (Table IX), particularly when one considers that many will wish to contribute only part of their time to screening work. If a high-quality service is to be achieved, training must be to the highest standards, with definition of how best the objectives of training can be assessed immediately following training and continuously thereafter. The maintenance of standards lies with the profession and, consequently, our professional organizations have a grave responsibility to ensure that these are defined and met.

The manpower resources indicated in Table IX cover only service requirements and not research. In the UK, we have an unparalleled opportunity to answer the questions posed in this lecture while establishing a model service and, through epidemiological studies, to gain new knowledge of the causative factors of breast cancer. We must not neglect this opportunity but continue to learn and advance knowledge, a message which I believe McKenzie Davidson would fully endorse. This is particularly relevant to those now starting out on their careers, who have the responsibility for safeguarding the quality of the screening service—for by so doing they will bring untold benefit to 25 000 women in the UK who, in each year, develop cancer of the breast.

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The use of real-time orbital ultrasound in Graves' ophthalmopathy: a comparison with computed tomography

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Abstract. Evaluation of the severity of orbital involvement and likelihood of the development of optic neuropathy in Graves' disease can be clinically difficult. We describe the use of real-time orbital ultrasound scanning to measure the medial rectus muscle width in 20 patients with Graves' ophthalmopathy and 21 normal individuals. The normal reference interval (to 2 SDs) was 1.75 to 4.07 mm. Significantly ($p < 0.001$; Mann Whitney *U*-test) larger values were observed in the patients compared with controls, and there was good correlation between medial rectus width and a clinical index of disease severity in individual eyes ($p < 0.001$; Spearman rank correlation coefficient). Comparison of the medial rectus measurements obtained using orbital computed tomography and ultrasound showed positive correlation at the $p < 0.001$ significance level. Computed tomographic medial rectus measurements also correlated with horizontal and vertical muscle indices for that orbit. We suggest that real-time ultrasound of medial rectus width, using widely available equipment, provides an accurate, simple and non-invasive means of evaluating the orbits of patients with Graves' disease. Repeated measurements may be of value in identifying patients at high risk of visual failure, and in following prospectively the orbital response to therapy in patients with Graves' ophthalmopathy.

The orbital complications of thyroid disease (Graves' ophthalmopathy—GO) present considerable difficulties in clinical management. Only 3–5% of patients with Graves' disease (GD) will develop sight-threatening complications such as optic neuropathy (ON), which may be a consequence of optic nerve compression by the enlarged extra-ocular muscles (EOM) that are characteristic of this condition (Gorman et al, 1984). However, it is clear that most GD patients develop changes of GO at some time during the course of their disease, the percentage rising to over 70% when sensitive diagnostic imaging techniques such as computed tomography (CT) are used (Forbes et al, 1986).

There are currently no reliable immunological markers of disease severity or activity and, although CT indices of EOM size have been used to define groups at high risk of developing ON, they do not appear to identify all patients at future risk of developing this complication if a single scan is used (Feldon & Weiner, 1982). Computed tomography cannot be used repeatedly as a routine investigation because of the radiation dose to the lens, and it is not always available outside major centres. We have used real-time orbital ultrasound scanning together with CT in a prospective study of GD patients. We examined normal individuals with ultrasound in order to define a normal range for medial rectus muscle width. We also assessed the relationship between CT and ultrasound measurements and related these measurements to a clinical index of disease severity.

Patients and methods

Twenty-one normal individuals (11 male, 10 female, aged 26 to 59 years) were recruited for orbital ultrasound scanning. Twenty patients who had been previously diagnosed as having Graves' disease on the basis of increased, diffuse uptake of technetium 99m on thyroid scanning, diffuse vascular goitre and biochemically confirmed hyperthyroidism underwent orbital CT and ultrasound scanning (four male, 16 female, aged 26 to 59 years). At the time of examination, seven patients were euthyroid and four hyperthyroid on treatment with carbimazole. Six patients had previously received radioiodine and three had undergone subtotal thyroidectomy; these patients were euthyroid and free of all thyroid medication. All those examined gave informed consent to the study.

The GD patients were assessed clinically at the time of orbital imaging by a single observer and the severity of their ophthalmopathy estimated using a clinical scoring system based on objective signs (Table I). Ophthalmoplegia was scored more highly in this system as this sign has previously been shown to carry more prognostic significance with regard to the risk of ON development (Sverker Hallin & Feldon, 1988a). Optic neuropathy was considered to be present if there was reduction in visual acuity, colour vision or visual fields that was not due to either anterior changes of GO or other disease processes.

Ultrasound and CT

Real-time ultrasound scanning was carried out on all subjects using a hand-held 7.5 MHz small-parts probe on a Diasonics DRF400 scanner. Ultrasound coupling gel was applied to the closed upper lid and the

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Table 1. Clinical assesment of GD patients

Sign	Score if present
Ophthalmoplegia	3
Periorbital oedema	1
Chemosis	1
Visible muscle insertion (medial or lateral rectus)	1
Injection of conjunctival vessels	1
Lid lag	1
Lid retraction	1
Proptosis 20–23 mm	1
Proptosis > 23 mm	2
Maximum score possible	11

Proptosis was measured clinically using the Hertel exophthalmometer by a single observer. The limbs of the instrument were positioned on the lateral orbital margins and brought into close approximation to the edge of the globe. Gentle backpressure was maintained to ensure that measurement errors due to periorbital tissue swelling were minimized.

maximum medial rectus thickness measured electronically while the subject maintained forward gaze. The medial rectus was the only muscle studied, as this proved to be the most easily and consistently visualized. The globe, optic nerve and retro-orbital tissues were also visualized to exclude other conditions.

The 20 GD patients were examined using a Somatom DRH scanner (Siemens) within 48 h of the ultrasound scan in all but two patients (when intervals of 2 and 3 weeks, respectively, elapsed between examinations). Data were acquired in the axial plane 15° inferior to the occipitomeatal baseline to give a plane parallel to the optic nerve using 2 mm (16 patients) or 4 mm (four patients) contiguous, non-overlapping slices. Patients were asked to maintain forward gaze and gentle eye closure during scans to prevent asymmetrical EOM contraction. Measurements of maximum medial rectus width were made on axial scans and proptosis assessed using the axial scan at the level of the optic nerve (Fig. 1). Axial data were post-processed to generate a coronal reconstruction scan in the plane transecting the optic nerves midway between the apex of the orbit and the back of the globe. This coronal scan was used to calculate horizontal and vertical muscle indices as described elsewhere (Barrett et al, 1988), giving a simple measure of extra-ocular muscle compression of the optic nerve space.

Statistical methods

Mann Whitney *U*-test, Spearman rank correlation and Deming regression analyses were used as stated in the text.

Results

For ultrasound measurements on normal subjects, no correlations were found between medial rectus width and height, weight, age or sex. Measurements were

normally distributed with a range of 1.7–4.0 mm, mean 2.9 mm and a normal reference interval (to 2 standard deviations (SDs)) of 1.75–4.07 mm.

There was highly significant ($p < 0.001$; Mann Whitney *U*-test) separation between medial rectus width in normals and in patients with GO of varying severity as judged by clinical scores (Fig. 2). Measurements of medial rectus width on ultrasound in GD patients correlated with the clinical score for that eye ($p < 0.001$; Spearman rank correlation coefficient) although some patients without clinical signs had evidence of significant muscle enlargement (Fig. 3). Plotting the medial rectus measurements obtained by CT against that from ultrasound showed significant correlation between the two values in individual orbits ($p < 0.001$, Deming regression) (Fig. 4). Measurements on CT of medial rectus width also correlated with the horizontal muscle index ($p = 0.017$, Spearman), the vertical muscle index ($p = 0.018$, Spearman) and with the sum of the muscle indices for the corresponding orbit ($p = 0.006$, Spearman).

Muscle indices of >67% were only seen in three orbits of the two patients where ON was demonstrated at the time of scanning. Computed tomographic measurements of proptosis were also compared with the clinical readings obtained by exophthalmometry. A correlation of $r = 0.916$ was obtained, using analysis of linear regression (data not shown).

Discussion

Graves' ophthalmopathy has a variety of clinical manifestations, but the most serious is visual loss, often due to ON. This may be diagnosed clinically in GO when there is evidence of optic nerve dysfunction as suggested by decreased visual acuity, visual field defects or diminished colour vision. Clinical diagnosis may be difficult, however, if the patient cannot co-operate with clinical tests (*e.g.* where massive periorbital oedema prevents lid opening) or where there is coexisting visual threat from another cause, such as corneal exposure.

Optic neuropathy can develop rapidly and is an ophthalmic emergency (Sergott & Glaser, 1981). Both medical and surgical therapy can be highly effective in restoring vision, particularly if therapy is instituted early. It is therefore vital to be able to predict which patients may be at greatest risk of developing ON, particularly as it is recognized clinically that ON may develop in the absence of marked external signs of GO.

Several publications have emphasized the role of orbital CT in this context (Enzmann et al, 1976; Forbes et al, 1986; Sverker et al, 1988b). Feldon et al (1985) demonstrated a quantitative relationship between EOM volume and risk of having ON or developing it during follow-up. They reported a disproportionate increase in medial rectus volume in their patients, as did Forbes et al (1986), who also suggested that orbital fat was increased, supporting the early work of Rundle and Pochin (1944) on autopsy specimens from GO patients. Barrett et al (1988) have devised a muscular index from coronal reconstructions to reflect EOM impingement on

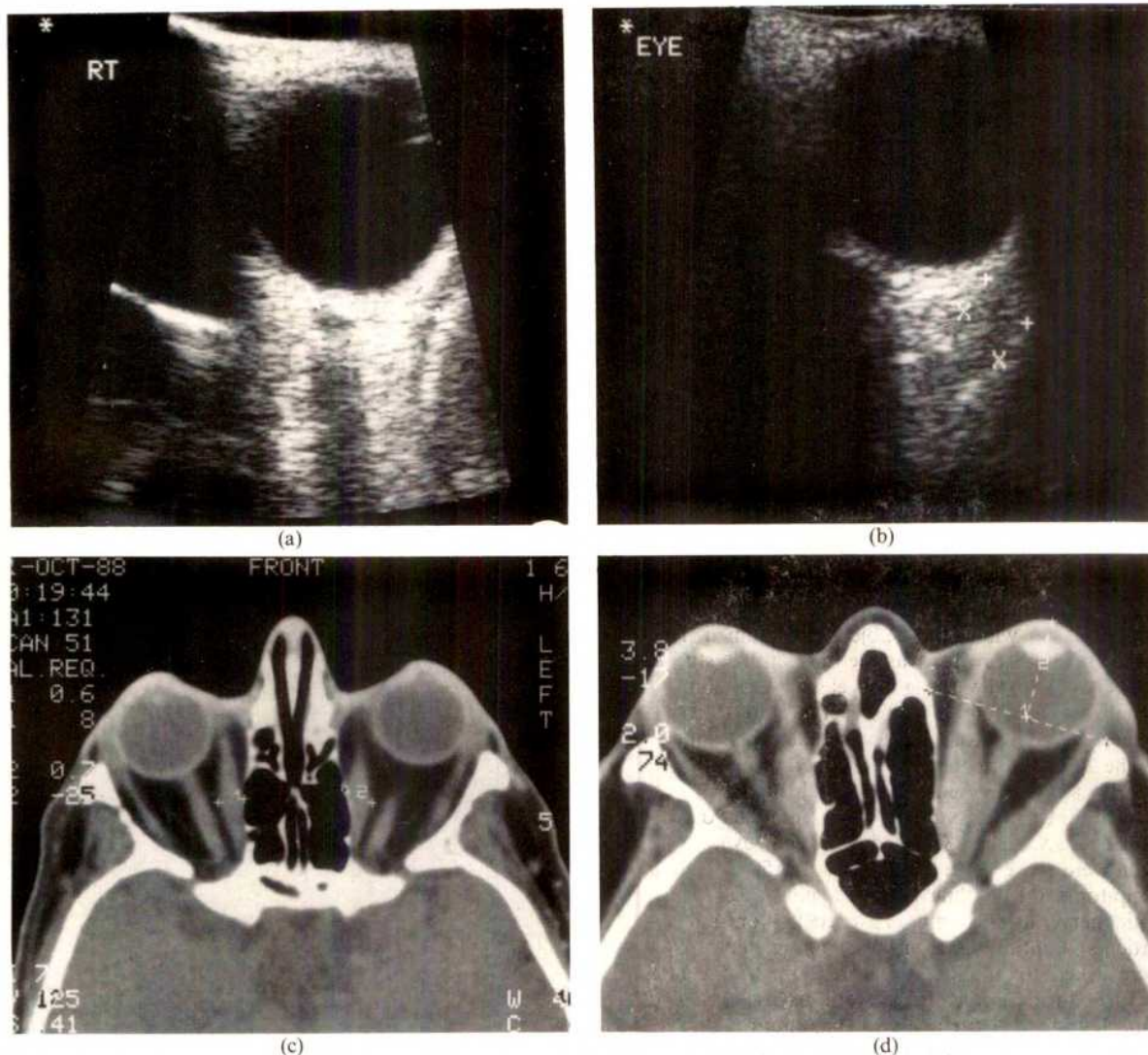


Figure 1. (a) Normal ultrasound appearance of the right eye. Note shadowing from the optic nerve posterior to the globe and the echo-poor band of the medial rectus (which has been measured) running parallel to the medial wall of the orbit. (b) Ultrasound appearance of the right eye in a patient with Graves' ophthalmopathy. The medial rectus is enlarged (width 0.6 cm) with irregularity of the internal echoes. (c) Axial CT scan of the right eye at the level of the optic nerve in the same patient as (b). The medial rectus is measured (D1=0.6 cm). (d) Axial CT scan at the level of the optic nerve of another patient with Graves' ophthalmopathy. This shows the method of measuring proptosis (D2=2.0 cm).

the optic nerve in a study of 31 GO patients. They suggested that muscular indices of $>67\%$ were diagnostic of ON. In our study, muscular indices of $>64\%$ were only seen in the presence of ON, lending further support to this suggestion.

In Barrett's series, 9% of orbits showed enlargement only of the inferior rectus, nevertheless Sverker Hallin and Feldon (1988b) have reported that CT medial rectus width shows a correlation of $r=0.8$ with total EOM volume and provides a simple way of assessing risk of ON development. Our own results also demonstrate that high muscle indices are found in the presence of

ON and that there is a significant correlation between CT measurements of medial rectus width and muscular indices.

Use of orbital CT axial scanning is, however, not without disadvantages; it delivers a radiation dose to the lens and is relatively time-consuming and costly. Patients may need repeated investigations over a prolonged period and the prevalence of GD means that large numbers of patients would require the examination. For these reasons, orbital ultrasound offers numerous advantages as an imaging technique in GO.

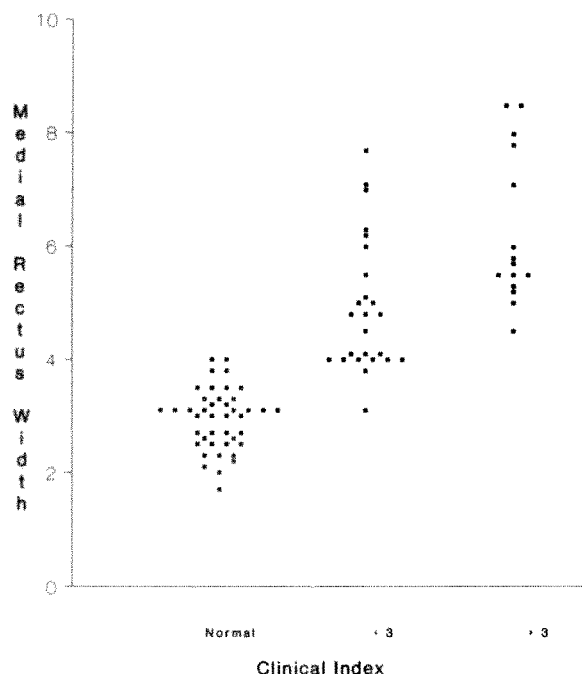


Figure 2. Medial rectus muscle width (mm) as measured by ultrasound shown in relation to the clinical state of the individual (normal volunteers and Graves' disease patients with scores on the index described in Table I of <3 or >3 , respectively). Correlation between medial rectus width and clinical index score was highly significant ($p < 0.001$; Mann Whitney *U*-test).

Both A- and static B-scanning are established techniques. Shamma et al (1980) used A-scanning in 14 patients with GO and found a characteristic appearance of muscle enlargement that was asymmetrical between the two orbits. McNutt et al (1977) carried out orbital A-scans in 52 normal subjects and reported maximum medial rectus width of 5.2 mm with a maximum difference between left and right orbits of 1.36 mm (95th centiles). This compares with normal maximum autopsy measurements of medial rectus of 3.5–6.0 mm (Sergott & Glaser, 1981). Werner et al (1974) showed muscle involvement in all but one of 47 GO patients using B-scanning, and Levine (1987) has described the A- and B-scan appearances of EOM in GO, with increased internal reflectivity and irregularity of internal echoes from affected muscles. Finally, Willinsky et al (1984) reported the use of real-time ultrasound scanning in GO, finding an upper limit of normal medial rectus width of 3.6 mm (95th centile) and larger muscles in most of their GO patients.

We report an upper limit of normal medial rectus width of 4.07 mm using real-time scanning. Our results also confirm that most patients with GO have enlarged medial recti on ultrasound and that the degree of enlargement correlates with both the clinical severity of

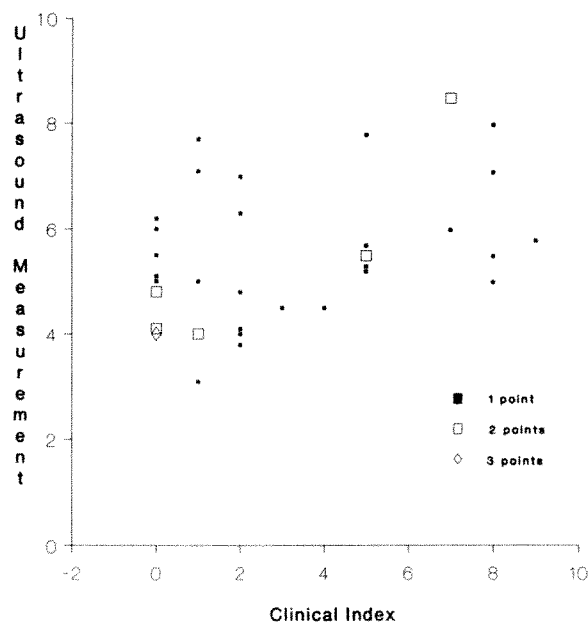


Figure 3. Relationship between ultrasound measurement of medial rectus width (mm) and clinical index score for that eye in Graves' disease patients ($p < 0.001$; Spearman rank correlation coefficient).

disease and measurements of width made on CT. It is therefore a valuable tool in the routine assessment of GD patients, using a rapid, non-invasive and simple radiological technique. The ability to perform repeated

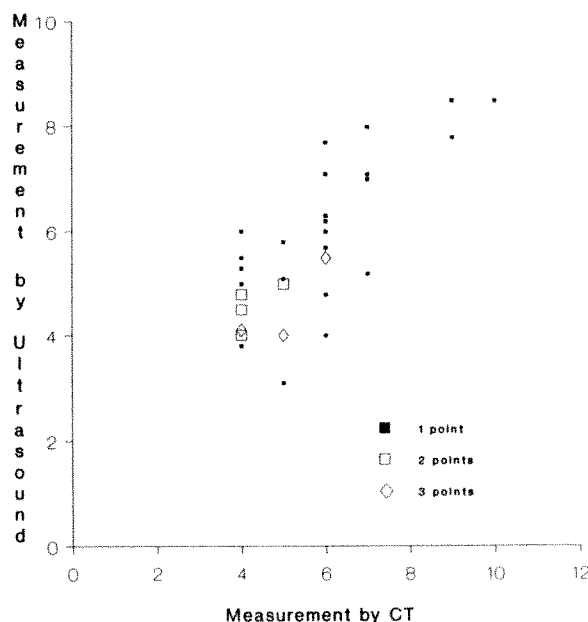


Figure 4. Comparison of results of medial rectus muscle width (mm) as measured by ultrasound and CT in individuals with Graves' disease ($p < 0.001$, Deming regression analysis).

examinations offers considerable scope for its use in research in this difficult field where, historically, there has been difficulty in interpreting the clinical significance of results obtained using subjective indices of disease presence and severity. We also suggest that real-time ultrasound could replace the routine use of CT in this condition, accepting that further work is required to define, using serial assessment, the precise ultrasound measurements that indicate those patients at high risk of ON development. Computed tomography would still be the method of choice in patients with ophthalmoplegia but normal medial rectus size, as these patients are likely to have involvement of only the inferior rectus. They may be missed if ultrasound is used unsupported by an initial CT scan. This group of patients is, however, likely to comprise less than 10% of all GD patients if currently published figures are representative.

Conclusions

Measurement of medial rectus width by real-time ultrasound scanning is a simple and non-invasive procedure that gives similar results to CT scanning. Medial rectus muscle width has previously been shown to correlate with the risk of development of optic neuropathy in Graves' disease. Ultrasound measurement of medial rectus muscle width is therefore a valuable technique for the prospective evaluation of patients with this condition.

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The anatomy of the first sacral nerve root sheath shown by computed tomography

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Abstract. Analysis of 25 patients with normal computed tomographic appearances at the lumbosacral junction revealed wide variation in the anatomical level at which the first sacral nerve root sheaths were seen emerging from the theca. In nine patients (36%), the S1 nerve root sheaths were first recognized at the level of the lumbosacral disc. In 14 patients (56%), the sheaths emerged cranial to the disc; it is possible that these patients may be more prone to neurological complications related to disc or facet joint disease, especially if the sheath is laterally sited within the lateral recess. Conversely, that minority of patients (two, 8%) in whom the root sheaths emerge caudal to the disc level may be relatively protected from neurological complications.

Low back pain with sciatica is a common symptom in the adult population. In patients below the age of 40 years, degeneration of intervertebral discs is the commonest cause (Macnab, 1977). Following such degeneration, herniation of the nucleus pulposus occurs commonly at the lumbosacral junction (Fries et al, 1982). The resulting pressure on the first sacral nerve by prolapsed or sequestered disc material is the usual cause of the symptoms and signs of root irritation.

Degeneration of the intervertebral facet joints is a more common cause of root irritation in patients over 50 years of age (Verbiest, 1954; Macnab, 1977). Hypertrophy of the articular processes causes narrowing of the lateral recess. This results in root entrapment, which is well shown by computed tomography (CT) (Stockley et al, 1988). Despite the excellent anatomical information now provided by modern radiological techniques, it is interesting that there is often poor correlation of clinical signs with anatomical abnormalities (Wiesel et al, 1984).

The lumbar and sacral nerve roots that form the cauda equina are arranged with increasing obliquity in the theca. The upper lumbar nerve root sheaths are often orientated almost at right angles to the theca and have relatively short intraspinal components (Crock, 1981). By contrast, the lower lumbar and first sacral nerve root sheaths arise from the theca at an acute angle and have increasingly longer intraspinal courses. Authorities vary as to the precise level of origin and course of the S1 nerve root sheaths; some cite the lumbosacral disc or the lower margin of L5 (Begg et al, 1946), whereas others state the level as the upper margin of S1 (Gado et al, 1984).

We have examined the origin of the S1 nerve root sheath as shown by CT in order to determine the

relationship to the level of the lumbosacral disc. In addition, the lateral course of the S1 root sheath was assessed with particular reference to location within the lateral recess.

Patients and methods

The hard copies of 97 consecutive lumbar spine CT examinations were reviewed. All patients with congenital skeletal abnormalities, abnormal lumbosacral discs or previous surgery were excluded. Twenty-five patients were considered to have normal appearances in the lumbosacral region and constitute the study group. There were 14 men (mean age 41 years, range 29-59 years) and 11 women (mean age 44 years, range 16-76 years).

All patients had been examined using a standard protocol (Dixon, 1983) on a Siemens Somatom 2 machine. The electronic data of the CT examinations in these 25 patients were retrieved and reviewed on the viewing console. It was observed on sequential images that the outline of the theca changed from a round or elliptical contour to a distinctly triangular contour immediately cranial to where the S1 nerve root sheaths could be identified as separate structures. The image where the shape changed to a triangular nature (*i.e.* immediately before the S1 sheaths could be identified as separate structures) was taken to be the origin of the S1 root sheath and the relationship to the disc was recorded (Fig. 1). In those patients in whom there was any discrepancy between the origins of the left and right sheaths, a mean level was assigned.

In those patients in whom the S1 root sheaths arose cranial to the disc, the position of the sheaths within the lateral recess was also recorded. A plane between the medial aspect of the L5/S1 facet joint and the "midpoint" of the cranial endplate of the body of S1 was selected. This "midpoint" was chosen to lie on the coronal plane passing through the anterior aspects of the sacral ala. The root sheaths were assessed as

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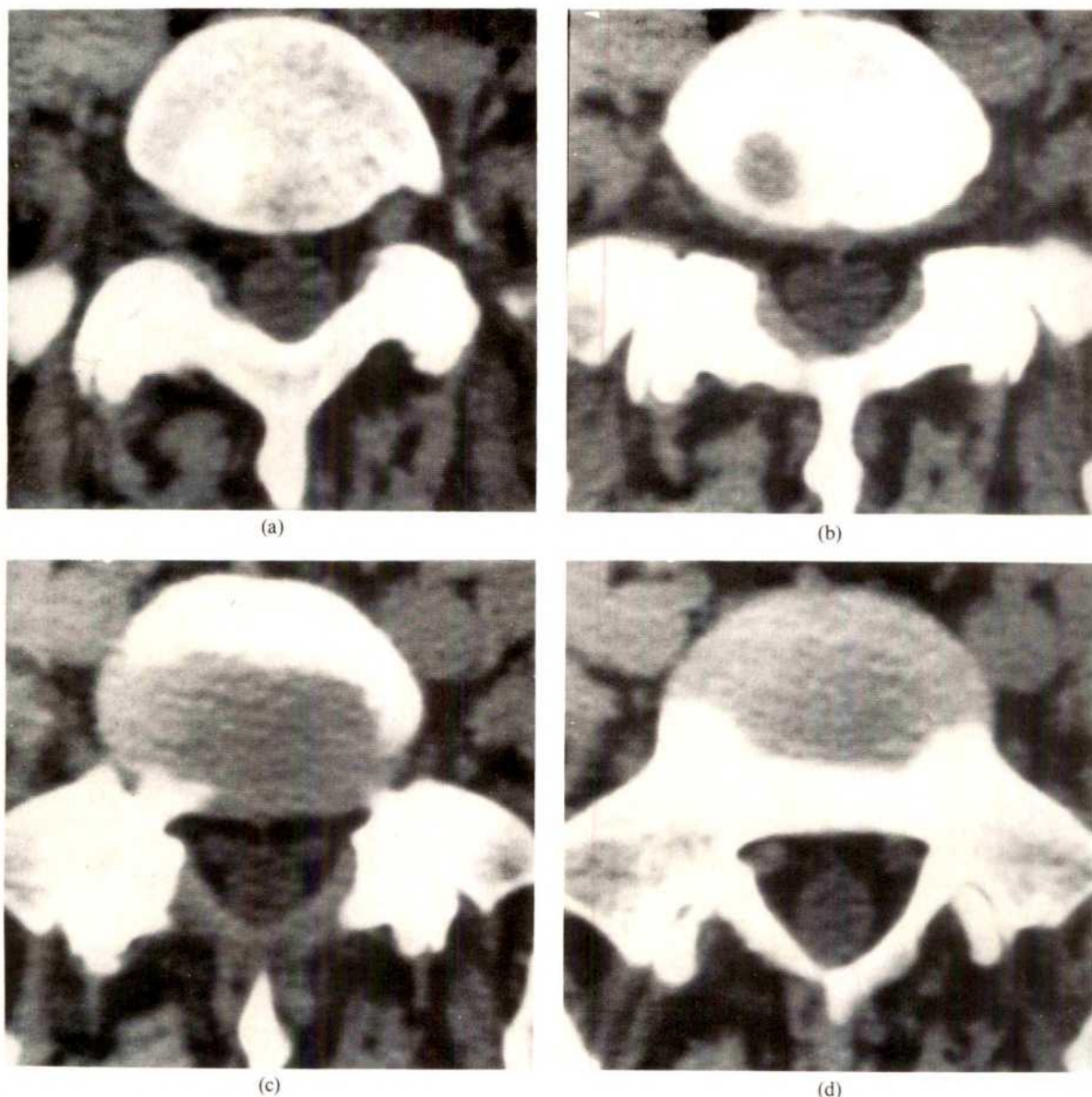


Figure 1. (a-d) Cranial to caudal. Sequence of images showing the change of shape of the theca from circular in (a) to triangular in (b). Fig 1b is taken to be the point of origin of the S1 nerve root sheaths as they are separate structures more caudally. The posterior aspect of the L5/S1 disc is best seen in (c) and a Schmorl's node is noted in (b).

medially or laterally sited according to their relationship to the facet joints (Fig. 2).

Results

The origins of the S1 nerve root sheaths are shown in Fig. 3. The results are expressed as distances above or below the disc in millimetres (mm). The mean distance from the disc was 3.5 mm cranial to the disc, and in the majority of patients (14 of 25, 56%), the S1 root sheaths originated cranial to the disc (see Fig. 1). The modal

point of origin (nine patients) was at disc level (Fig. 4). There were two cases where the S1 root sheaths were not identified separate from the theca until caudal to the lumbosacral disc (Fig. 5). Only in two patients was there any asymmetry in the origins of the left and right root sheaths. The maximum discrepancy was 5 mm; no case of conjoined root was seen.

Figure 6 shows the relationship of the S1 root sheaths to the L5/S1 facet joints in those 14 patients whose root sheaths originated cranial to the lumbosacral disc.

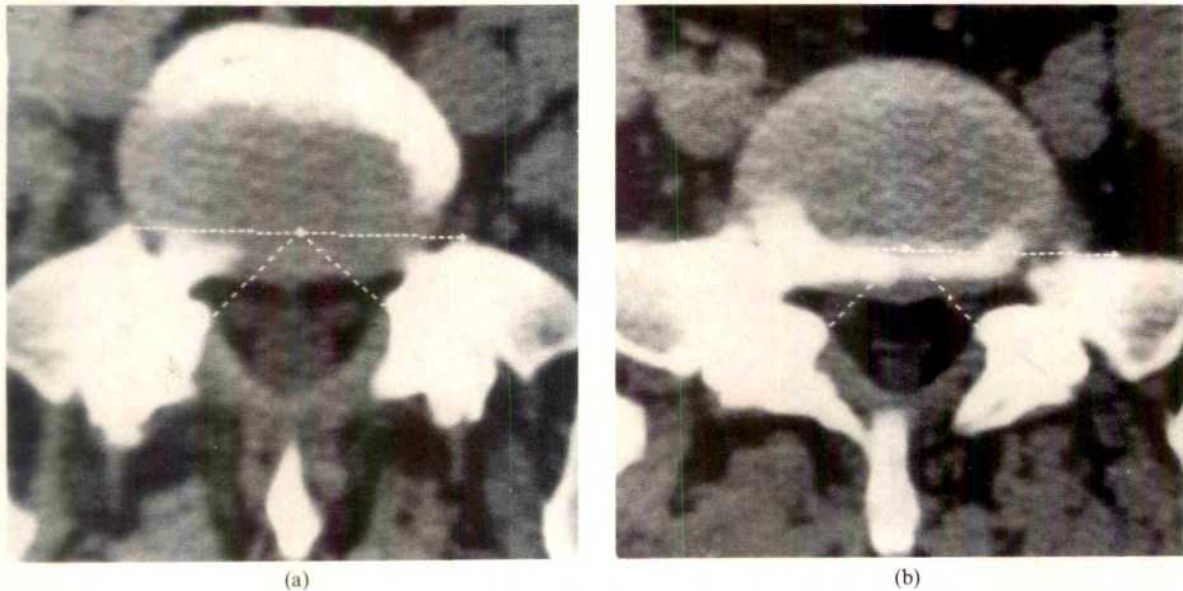


Figure 2. Classification of the position of the S1 nerve root sheaths in the lateral recesses (see text). Sheaths lying medial to the reference line as in Fig. 2a were classed as "medial"; those on, or lateral to, the line (Fig. 2b) were classed as "lateral".

CRANIAL

+20

+

+15

+

+10

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+5

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DISC

+ + + + + + + + +

+

-5

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CAUDAL

Discussion

This study has shown that there is considerable variation in the anatomical level at which the origin of the S1 nerve root sheaths can be recognized on CT. In 23 of 25 patients (92%) these root sheaths appeared to emerge at (nine, 36%), or cranial to (14, 56%), the lumbosacral disc. The intraspinal components of the root sheaths above the disc may be of considerable length (18 mm in one case). Of those cases in whom the root sheaths emerged cranial to the disc, the mean distance of the point of origin was 7 mm from disc level. In patients with this anatomical arrangement (14 of 25), the S1 nerve roots are likely to be more susceptible to disc protrusions or cranially directed sequestrations than those whose S1 root sheaths emerge at or caudal to the disc. Given their longer intraspinal course, it might be expected that these sheaths follow more lateral courses within the extrathecal fat. In six of these 14 patients the S1 root sheaths were considered to be laterally sited within the lateral recesses as defined above. These nerve roots would be prime candidates for entrapment by facet joint osteophytosis alone or in combination with minor disc protrusions. Such arrangement could be regarded as "unfavourable" anatomy.

Figure 3. A chart showing the craniocaudal origin of the nerve root sheath with reference to the L5/S1 disc in the full series of 25 patients.

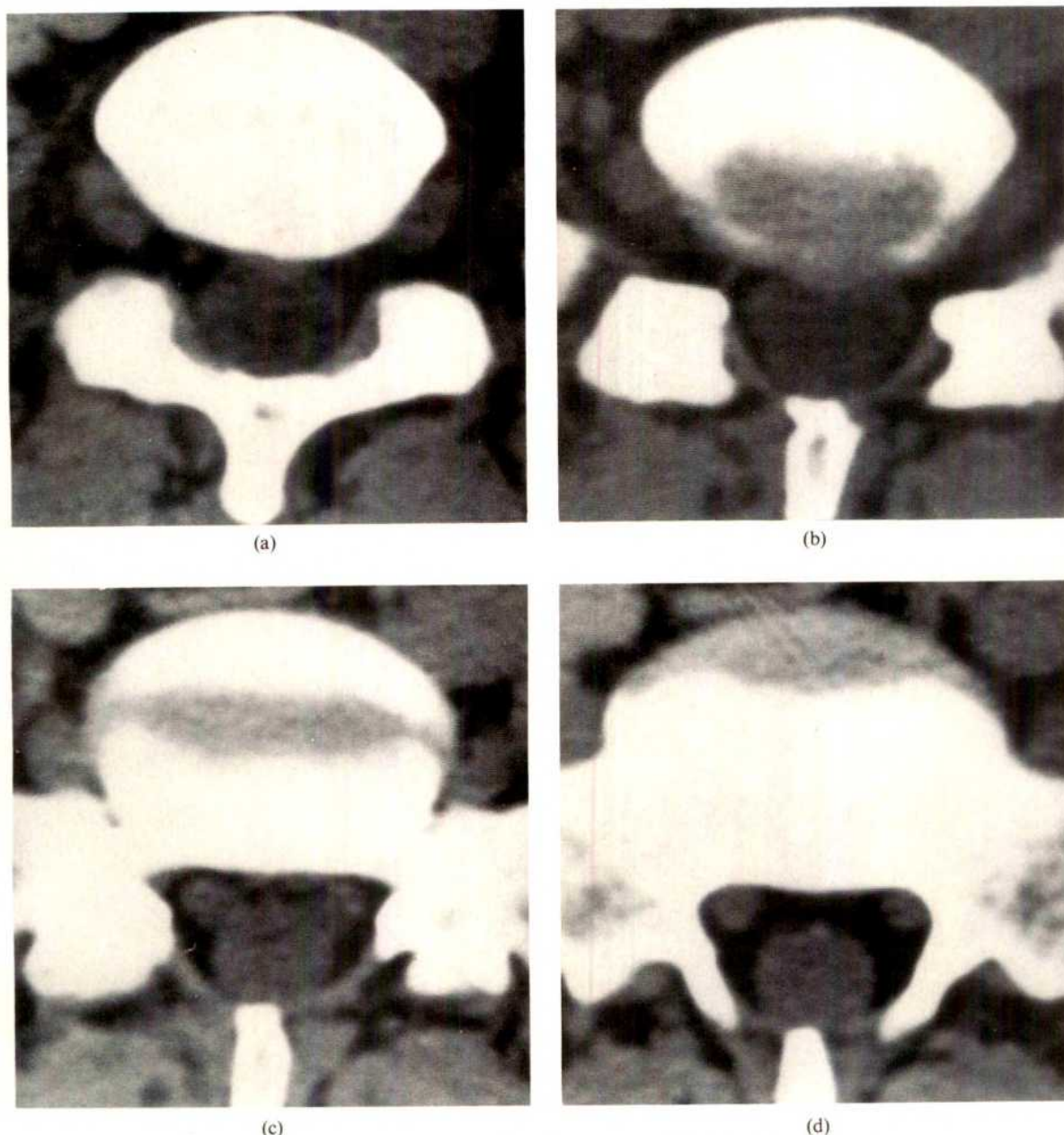


Figure 4. (a-d) Sequence of images showing the point of origin of the S1 nerve root sheaths at disc level (b).

At the other end of the range of appearances, there were two patients (8%) in whom the S1 root sheaths were not seen separately from the theca until caudal to the L5/S1 disc (Fig. 5). These root sheaths therefore had relatively short intraspinal courses before reaching the intervertebral foramina. It is tempting to suppose that, in these patients, root irritation due to disc disease could only be produced by large, caudally directed protrusions or sequestrations. This arrangement is thus considered

more "favourable" in so far that the sheaths are less likely to be affected by the common degenerative diseases.

These conclusions, drawn from the evidence presented, are open to many criticisms. The first is that the fluid-filled thecal sac and the separate root sheath may run more closely together in some patients than in others. In those where the root sheaths and theca are closely opposed, it is possible that the sheaths are not

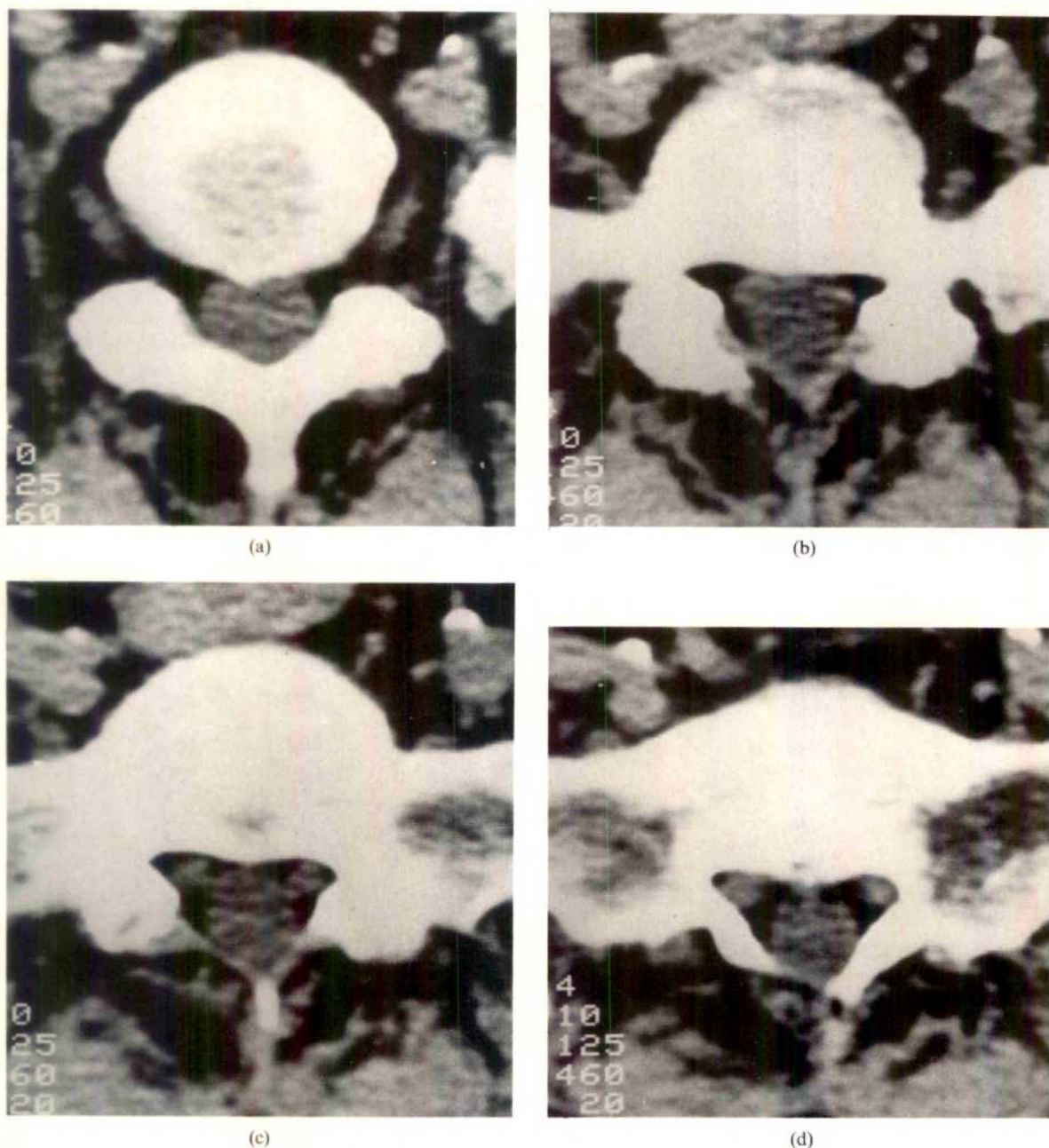


Figure 5. (a-d) Sequence of images showing the point of origin of the S1 nerve root sheaths (b) caudal to the L5/S1 disc.

seen as separate structures for some distance caudal to the true origin. However, the change in shape of the thecal sac provides some evidence of a definite pattern to the emerging sheath, reducing the likelihood of erroneous measurement.

The measurements are inevitably affected by the increments used between CT images. They will be more accurate in those patients where intervening images were

used over and above the routine increments of the standard protocol.

The sheaths themselves are only demonstrated by virtue of surrounding epidural fat, which in itself is a very variable entity (Dixon, 1986). In those patients with less epidural fat, the sheaths might appear to emerge more caudally. The case shown in Fig. 5 would appear to refute this possibility as here the sheaths are

Despite these possible criticisms, we consider that the presence of favourable anatomy of the S1 root sheaths

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Outpatient lumbar radiculography: comparison of iopamidol and iohexol and a literature review

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Abstract. A prospective study of 261 patients undergoing lumbar radiculography using 12 ml iopamidol (200 mgI/ml) was undertaken to determine whether the procedure could be performed safely on an outpatient basis. No statistically significant differences in the incidence and severity of side-effects were found between the 132 outpatients and 129 inpatient controls. Nine outpatients had to be kept in hospital at the end of a 4-h observation period and a further two outpatients were re-admitted to hospital because of severe side-effects. The current study was compared with a preceding study of identical design, already published, in which 200 patients underwent lumbar radiculography with 10 ml iohexol (240 mgI/ml). No statistically significant differences in the incidence and severity of side-effects between the two contrast media were evident up to 24 h after the examination. In the period between 24 h and 7 days, the incidence and severity of headache, nausea and dizziness were all significantly greater in the iopamidol group. Although outpatient radiculography can be performed safely with both contrast media, the higher incidence of delayed side-effects in the iopamidol patients prompts the authors to express a preference for iohexol for intrathecal use. The increased incidence of adverse reactions in female patients and the literature comparing iopamidol and iohexol for myelography are discussed.

Since a rapid return to normal activity following lumbar radiculography, as an alternative to bedrest, is not associated with an increased incidence of side-effects (Robertson et al, 1980; Carbaat & van Crevel, 1981; Gulati et al, 1981; Sykes et al, 1981; Macpherson et al, 1983; Macpherson & Teasdale, 1984; Kuuliala & Goransson, 1987), it has proved possible to perform the examination on an outpatient basis. This practice reduces considerably the costs of radiculography and has been employed using the various contrast media available: meglumine iocarmate (Dimer X, Guerbet) (van Niekerk, 1979), metrizamide (Amipaque, Nyegaard) (Kausch, 1981; Kushner et al, 1983; Tate et al, 1985; Zinreich et al, 1985; Kostiner & Krook, 1985; Badami et al, 1986) and iopamidol (Niopam, Bracco) (Postacchini & Massobrio, 1985; Andreula et al, 1987). More recently, iohexol (Omnipaque, Nycomed) has also been shown to be safe for use in outpatient radiculography (Skalpe & Nakstad, 1988; Davies et al, 1989), although in the earlier of the two studies the outpatients were discharged to other hospitals rather than their respective homes.

Direct comparison of the incidence and severity of side-effects following radiculography between various studies is of limited value because of the multiple different variables inherent in every study. None of the previous publications on outpatient lumbar radiculography has attempted to compare the efficacy of more than one contrast medium in that particular context. The purpose of the present prospective study

was to determine the incidence and severity of side-effects following lumbar radiculography with iopamidol in similar outpatient and inpatient groups and to compare the results with those already published for iohexol (Davies et al, 1989). In both studies the source of the patients and design of the study were identical.

Patients and methods

Four hundred and sixty-one patients referred for lumbar radiculography from orthopaedic outpatient clinics were prospectively allocated to either outpatient or inpatient control groups. The first 200 patients (100 male and 100 female; 99 outpatients and 101 inpatients) underwent the examination with 10 ml iohexol (240 mgI/ml) (Davies et al, 1989). In order that the overall dose of iodine should remain the same (2.4 g), the 261 patients studied consecutively (150 male and 111 female; 132 outpatients and 129 inpatients) were given 12 ml iopamidol (200 mgI/ml).

In order to minimize the effects of other factors, the criteria for patient selection/exclusion, pre- and post-procedural care and advice and the gauge of the lumbar puncture needle (22-gauge disposable spinal needle) were identical for all 461 patients. Outpatients required a driver to transport them on the day of the examination, a reliable person at home to monitor them until the following morning and access to a telephone should the need to obtain medical advice arise.

All patients were required to complete four questionnaires, before, 4 h, 24 h and 1 week after the examination, in which they were asked to make a subjective assessment as to the presence and severity of any side-effects experienced. Provided their condition allowed, the outpatients were sent home after an initial

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observation period of 4 h, whereas the inpatients remained in hospital for a minimum of 24 h.

Further details regarding the design of the study are included in the published results of the 200 patients undergoing radiculography with iohexol (Davies et al, 1989).

Criticism may be made that the two studies were conducted consecutively and not concurrently. Since, however, the design of the study remained the same and there is no reason to believe that the sample of patients differed in any significant manner, valid comparisons between the two contrast media can be made. The results are based entirely on the subjective assessments by the patients themselves, thereby rendering irrelevant the radiologists' knowledge of which contrast medium was being used.

Results

The incidence (*i.e.* percentage patients experiencing side-effects) and severity of side-effects (headache, nausea, vomiting and dizziness) before, 4 h, 24 h and 1 week following lumbar radiculography for iohexol and iopamidol are summarized in Figs 1 and 2, respectively. The results given at 1 week include all side-effects experienced between the end of the 1st and 7th day inclusively. It was demonstrated that there was no statistically significant difference in the incidence and severity of any side-effects between the outpatient and inpatient control groups for either contrast medium. The maximum incidence of side-effects in the iohexol group occurred within the first 24 h, with headache the most common symptom (42%). Headache was also the most common adverse symptom in the iopamidol group, but the highest incidence (45%) was after the 1st day (Fig. 2).

At the end of the 4 h observation period, three (3%) of the iohexol and nine (6.8%) of the iopamidol outpatient groups were kept in hospital because of the rapid onset of severe side-effects. At 24 h, seven (6.9%) of the iohexol and 16 (12.4%) of the iopamidol inpatient groups were kept in hospital because of side-effects. Following discharge from hospital, 14 (7%) patients from the iohexol group (13 outpatients and one former inpatient) and 26 (10%) from the iopamidol group (21 outpatients and five former inpatients) telephoned the hospital for medical advice. Of these, three from the outpatient and one from the inpatient iohexol groups were subsequently re-admitted to hospital for observation. Only two iopamidol patients, both initially outpatients, had to be re-admitted but one of these, a 46-year-old woman, had to be hospitalized twice, 14 and 25 days after the examination. A precautionary diagnostic lumbar puncture showed a mildly elevated cerebrospinal fluid white count consistent with a residual meningitic irritation.

As there were no statistically significant differences in the incidence and severity of side-effects between the outpatient and inpatient controls for either iohexol or iopamidol (Figs 1, 2), the two groups for each contrast medium were combined and comparison of the two

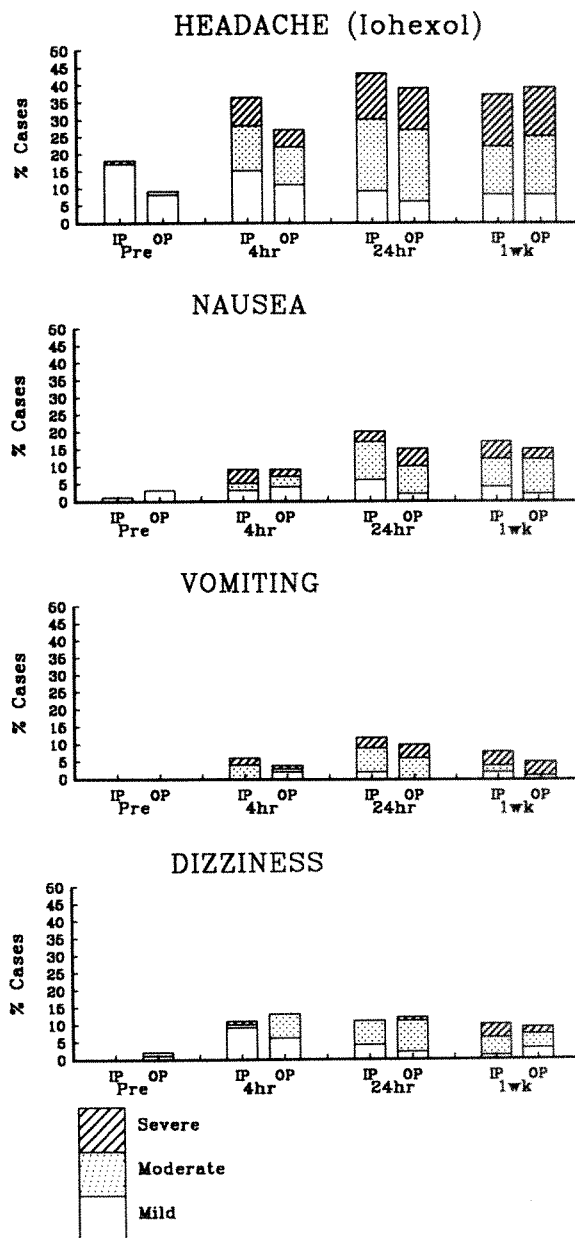


Figure 1. Adverse reactions in the inpatient (IP) and outpatient (OP) groups undergoing radiculography with iohexol.

larger samples performed (iohexol: $n=200$, iopamidol: $n=261$). The incidence and severity of adverse reactions for the overall iohexol and iopamidol groups are shown in Fig. 3. No statistically significant differences were demonstrated before, 4 h or 24 h after the examination. However, analysis of the patients' responses from the 24 h questionnaire regarding the onset of side-effects revealed a significantly more rapid onset of both headache ($p=0.01$) and nausea ($p<0.05$) in the

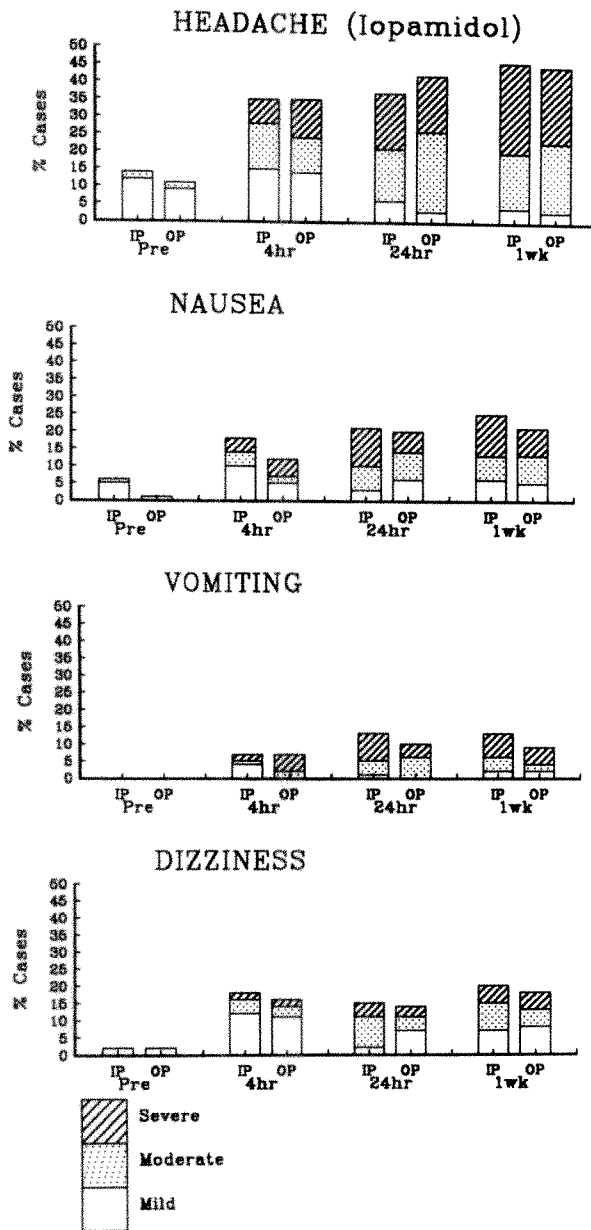


Figure 2. Adverse reactions in the inpatient (IP) and outpatient (OP) groups undergoing radiculography with iopamidol.

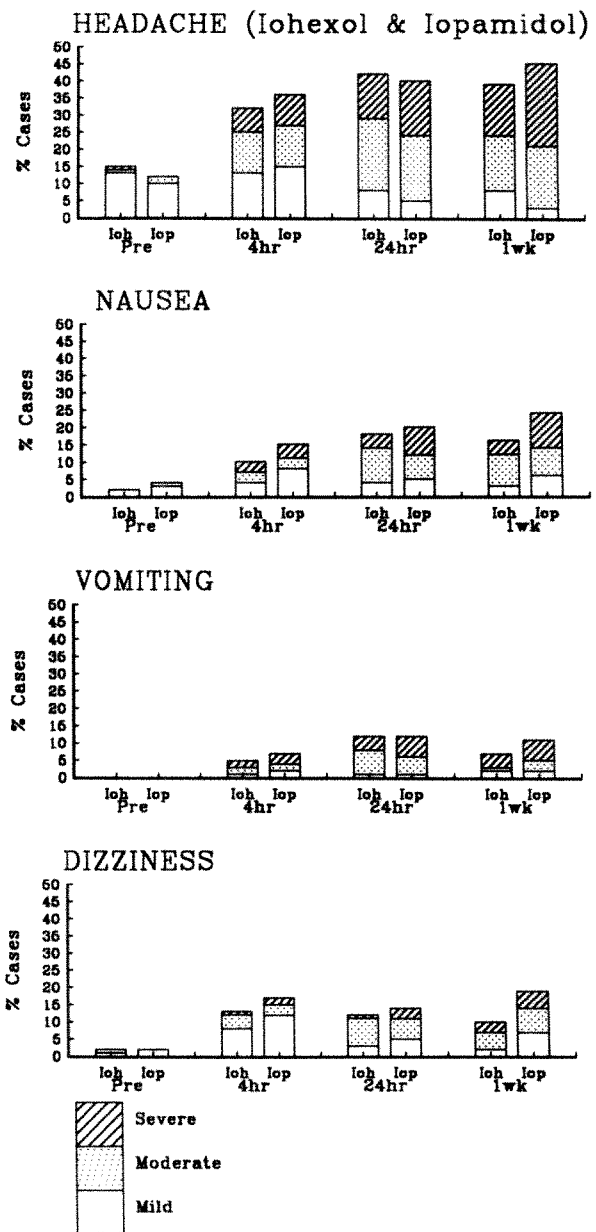


Figure 3. Comparison of adverse reactions following radiculography with iohexol (Ioh) and iopamidol (Iop).

iopamidol group (Fig. 4). Also in the iopamidol group, at 24 h, the duration of headache ($p=0.02$) and dizziness ($p=0.02$) were significantly greater (Fig. 5).

Analysis of the results of the final questionnaire demonstrated that in the period between 24 h and 7 days after the examination, the incidence and severity of headache ($p=0.01$), nausea ($p=0.03$) and dizziness ($p=0.02$) were all significantly greater in the iopamidol group (Fig. 3). Although the differences in the rate of onset of headache and nausea were shown to be

significant in the first 24 h, this was not the case in the onset of any side-effects after the first day (Fig. 6). The duration of nausea, vomiting and dizziness after the first day were shown to be similar for both groups with only the duration of headache being significantly greater in the iopamidol group ($p=0.05$) (Fig. 7). Of those patients with headache, a duration of 1 week plus was found in one-third of iopamidol and one-sixth of iohexol patients (Fig. 7).

Analysis of the data by sex of the patients revealed a

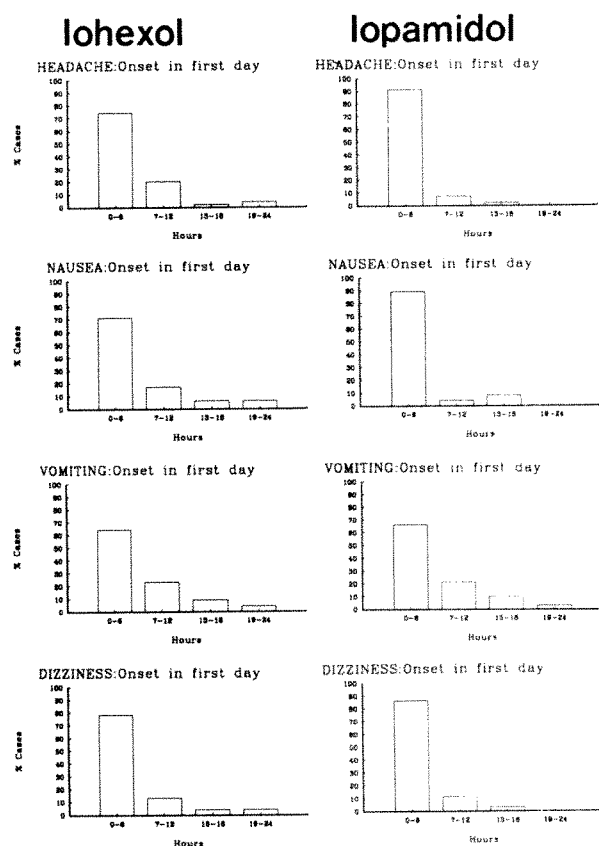


Figure 4. Time of onset of adverse reactions during the first 24 h after radiculography.

consistently higher occurrence of symptoms in the female patients for both contrast media (Figs 8, 9). The differences in the incidence and severity of side-effects between the sexes was significantly greater in the iohexol group for headache at 24 h ($p=0.008$) (Fig. 8) and in the iopamidol group for all four documented side-effects, 4 h, 24 h and 1 week after the examination (Fig. 9). No significant differences were demonstrated between the sexes in the onset or duration of side-effects for either contrast medium.

Similar numbers of men and women were present in the small group of outpatients who were either retained in hospital after the 4-h observation period or were subsequently re-admitted because of severe side-effects. Women, however, were twice as likely as men to telephone the hospital for medical advice, and, in the inpatient group, twice as likely to be kept in hospital after 24 h because of adverse reactions.

Discussion

In those hospitals where access to computed tomography and magnetic resonance is limited, lumbar radiculography remains the investigation of choice for sciatica. Performing the examination on an outpatient

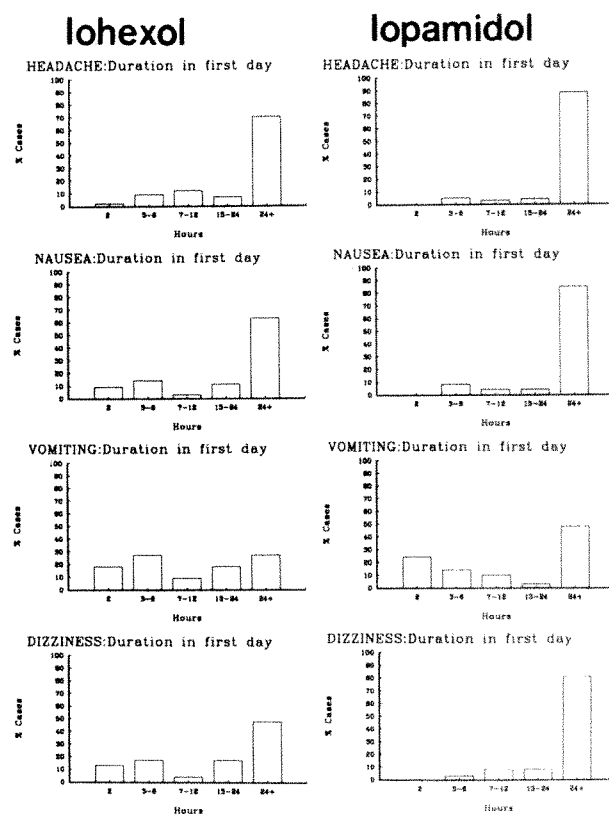


Figure 5. Duration of adverse reactions commencing in the first 24 h after radiculography.

basis results in obvious financial savings as well as indirectly increasing the availability of orthopaedic beds. This study confirms previous published reports that outpatient radiculography can be performed safely with iopamidol (Postacchini & Massobrio, 1985; Andreula et al, 1987) and reiterates the earlier similar findings with iohexol (Davies et al, 1989).

It is well recognized that both intrathecal iopamidol and iohexol are better tolerated than the original non-ionic contrast medium, metrizamide (iopamidol: Bassi et al, 1982; Bockenheimer & Hillesheimer, 1983; Lamb & Holland, 1983; Peeters et al, 1983; McAllister & Hall, 1983; Stoddart & Watt, 1984; de Villiers et al, 1984; iohexol: Eldevik et al, 1983; Kendall et al, 1983; Batty, 1984; Kendall & Stevens, 1984; Burrows, 1984; Kieffer et al, 1984; Lilleas et al, 1986) and perform well radiographically.

Relatively few comparative studies of iopamidol and iohexol following myelography have been published and with mixed results. Two studies found that iohexol was tolerated better than iopamidol (Lamb, 1985; Broadbridge et al, 1987), three that the side-effects were equivalent (Molyneux et al, 1983; Macpherson et al, 1985; Valk et al, 1987) and one found in favour of iopamidol (Hoe et al, 1986). In this study, despite the fact that the patients were not allocated one or other

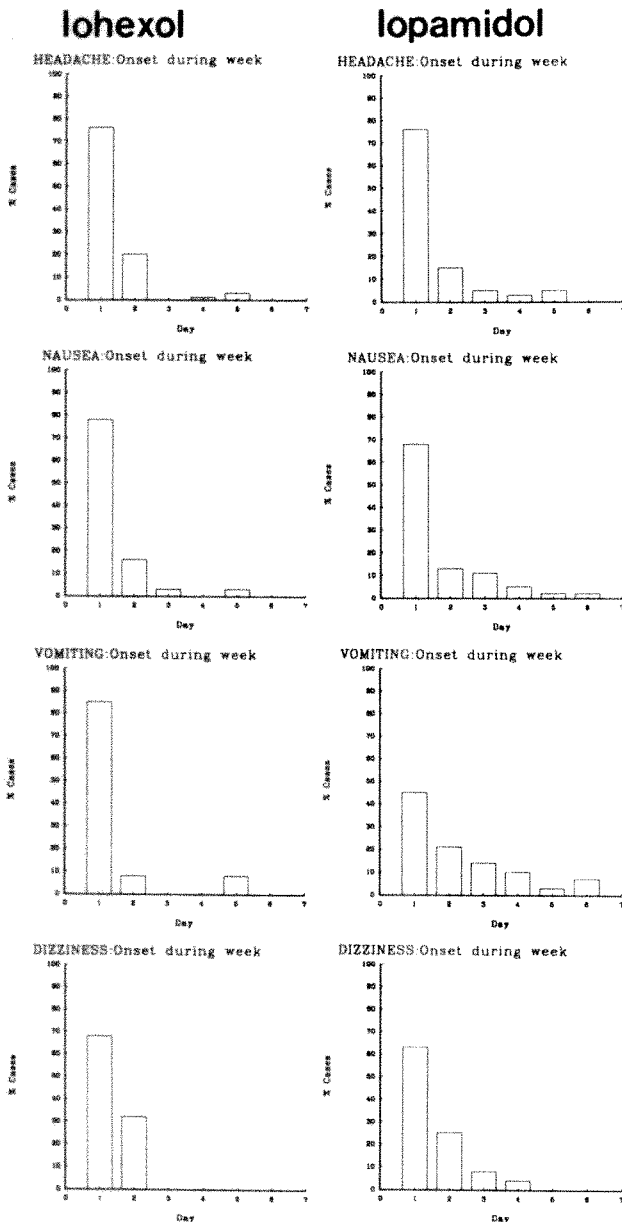


Figure 6. Day of onset of adverse reactions following radiculography.

contrast medium on a blind basis, valid comparison can be made as the results are based solely on the subjective assessment by the patients in answering a series of identical questionnaires. This series, comprising 461 patients, forms the second largest published comparison of iopamidol and iohexol for radiculography. Broadbridge et al (1987) include in their paper on 50 patients assessed with visual evoked responses, their experience of a further 600 examinations on unselected patients.

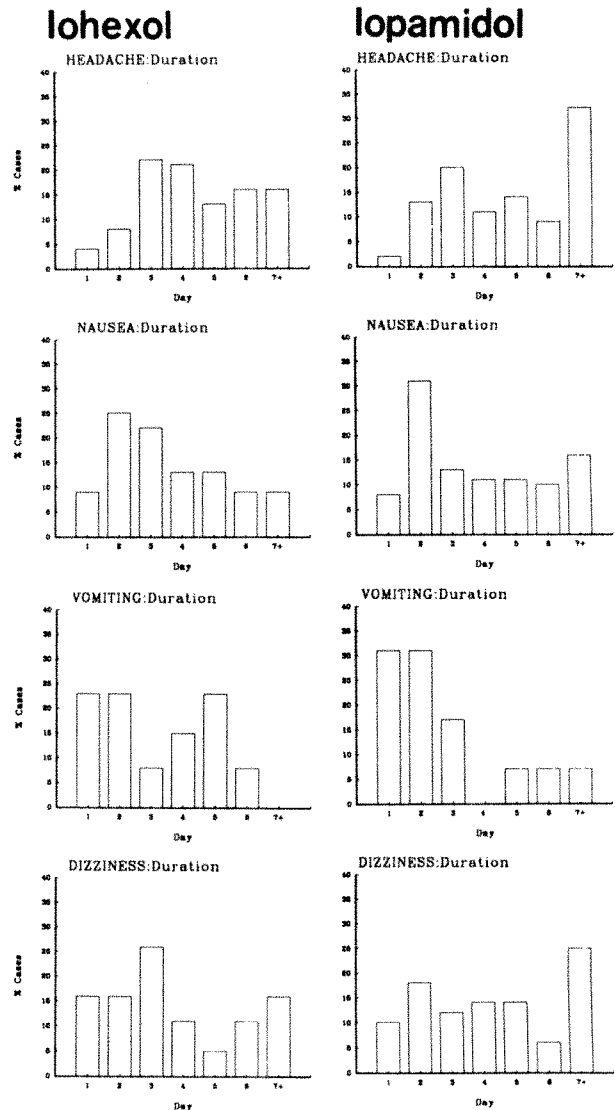


Figure 7. Duration of adverse reactions in the week following radiculography.

The principal conclusion of the present study is that outpatient radiculography is safe with both contrast media; however, in certain particular aspects, iohexol was significantly better tolerated than iopamidol. It is a simple maxim of statistical analysis that the larger the sample the greater the degree of confidence in the results. It is interesting to note, therefore, that the three studies, including this paper, which consider iohexol less toxic than iopamidol comprise in excess of 1400 examinations whereas the remaining four studies, in which the incidence of adverse reactions was similar or less with iopamidol, includes in total fewer than 300 patients.

Most reports only formally monitored the patients for 24–48 h after myelography. Several studies left the onus

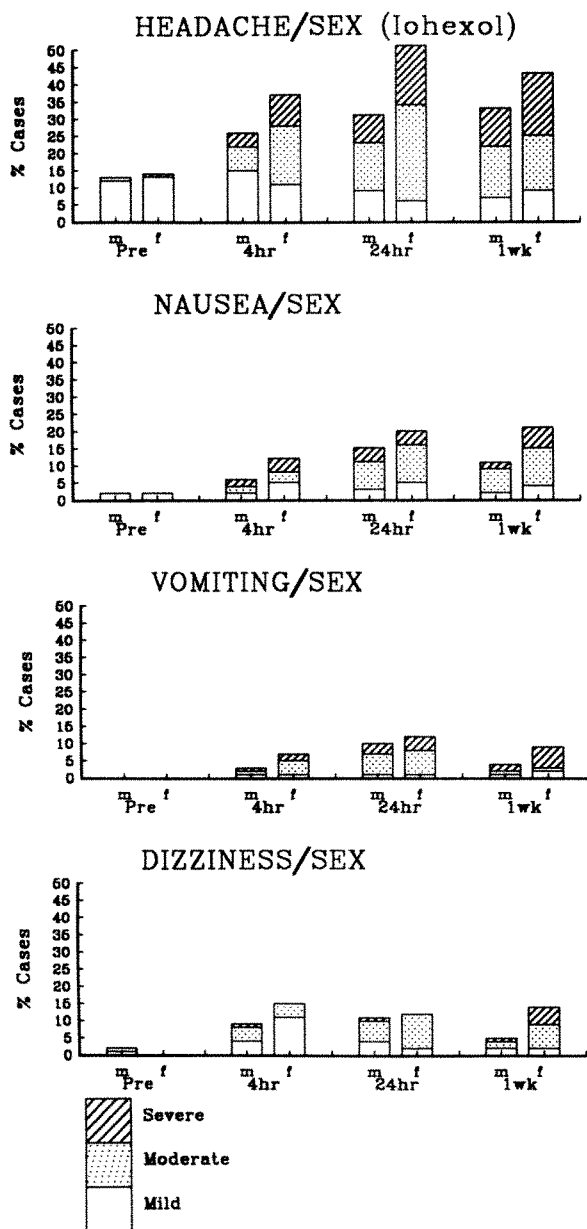


Figure 8. Adverse reactions in male (m) and female (f) patients undergoing radiculography with iohexol.

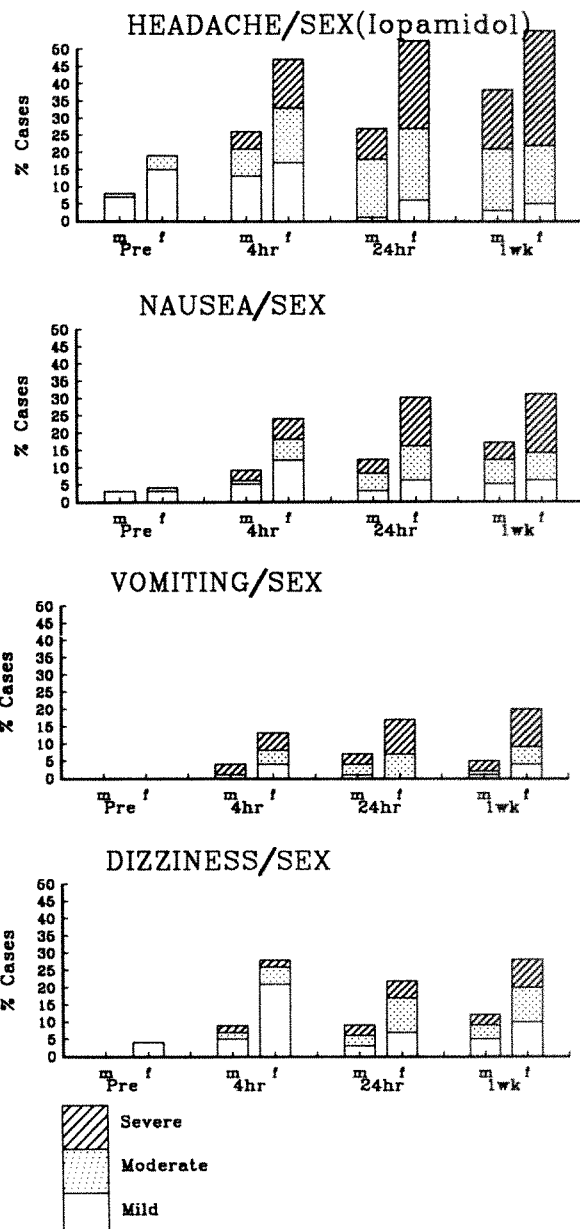


Figure 9. Adverse reactions in male (m) and female (f) patients undergoing radiculography with iopamidol.

on the patients themselves to keep in touch with the hospital (Milette et al, 1983; Stoddart & Watt, 1984; Kuuliala & Goransson, 1987) or only contacted those who already had symptoms within the first couple of days (Lamb, 1985; Badami et al, 1986). If the current study had been based solely on the results of the 4- and 24-h questionnaires, the conclusions would have agreed with those of Molyneux et al (1983), Macpherson et al (1985) and Valk et al (1987) and showed that there was

no significant difference in the incidence and severity of side-effects between the contrast media. Lamb (1985) noted a slightly earlier onset of headache with iohexol, which differs from this study, which found a more rapid onset with iopamidol of both headache and nausea within the first 24 h (Fig. 4). This finding might explain that, although the incidence and severity of side-effects within the first day were similar, a higher proportion of iopamidol patients in this study were kept in hospital.

It is during the period between the first day and 1 week after the examination that the differences between the contrast media become apparent. The authors are aware of only one previous non-comparative study with iohexol in which all patients routinely completed a questionnaire at 1 week, as in this study (Skalpe & Nakstad, 1988). This paper showed that 30 to 40% of headaches commenced more than 24 h after myelography and therefore concluded that a "follow-up period of several days is essential for evaluation". Approximately one-quarter of the side-effects experienced in this study started after the first day (Fig. 6) and during this period the incidence and severity of headache, nausea and dizziness were significantly greater in the iopamidol group (Fig. 3).

This study also demonstrates, as in most previous reports, an increased incidence of adverse reactions in women, particularly significant in the iopamidol patients (Fig. 9). Indeed, had there not been a minor preponderance of men in the iopamidol group, it might be expected that the differences between the contrast media would have been more pronounced. The minor female bias in side-effects even before the examination was performed (Fig. 9) suggests that the difference between the sexes might, at least in part, be a question of perception and not wholly a physiological response to the contrast medium.

The quoted incidence of side-effects with both contrast media varies enormously between different reports from as low as 15% headaches (Kendall et al, 1983) to 40% with iohexol (Simon et al, 1987) and 58% with iopamidol (Kleefield et al, 1983). These differences can be explained by the fact that no two studies are identical in design. Important factors include volume and concentration of contrast medium, gauge of spinal needle, proximal extent of the contrast medium in the spinal canal and the nature of the assessment of reactions and aftercare.

How much the lumbar puncture itself contributes to the side-effects is difficult to ascertain. In their studies following lumbar puncture alone, Tourtellotte et al (1972) and Carbaat and van Crevel (1981) found an incidence of headache of 36 and 37%, respectively, both of which levels are considerably higher than that quoted in numerous studies where contrast medium was subsequently injected. To conclude that the contrast medium might actually have a protective effect would obviously be fallacious and the large range of results only serves to highlight the imprecise nature of subjective assessments.

A few studies have introduced objective testing in the form of electroencephalograms (Kendall & Stevens, 1984; Nakstad et al, 1984; Lamb, 1985; Macpherson et al, 1985) or measurement of visual evoked responses (Molyneux et al, 1983; Broadbridge et al, 1984, 1987). Not all these studies were comparative but the general trend in the results is that, where there is a demonstrable difference between the contrast media, it is iohexol that appears less neurotoxic. The weight of evidence, corroborated by this study, indicates that there is a

gradual, but perceptible, shift in favour of iohexol as the contrast medium of choice for intrathecal use.

Whilst outpatient radiculography has benefits for both the patient and the hospital, this study indicates that a limited number of outpatients (6% of iohexol and 8.3% iopamidol outpatients) will require admission because of adverse reactions. Although the medical treatment for the vast majority of side-effects is principally supportive, it must be remembered that severe idiosyncratic reactions may occur with both iopamidol (Waller & Chaudhuri, 1985; Carchietti et al, 1988) and iohexol (Brown & Murphy, 1985; Donaghy et al, 1985) or simply following lumbar puncture alone (Dohrmann et al, 1983; Hart et al, 1988). It is therefore important that all patients should have a reliable person at home and access to a telephone and be advised as to whom to contact should the need arise (Stoddart & Watt, 1984). Medical staff should also be warned that if there is any doubt as to the patient's condition, admission to hospital should be arranged without delay.

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Dysphagia after fast neutron therapy to the head and neck

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Abstract. Nine patients presenting with dysphagia following successful treatment for head and neck cancer with neutron radiotherapy are reviewed. Combined clinical and videofluoroscopic investigation is used to analyse their deficits and provide indications for management. All patients show impairment of both the oral and pharyngeal phases of the swallow, with the exception of one subject who shows signs of focal neurological damage. It is suggested that fibrosis is the underlying cause of dysphagia in the remainder.

For over 50 years, neutrons have been used as an alternative to conventional radiotherapy in the treatment of slow-growing and advanced tumours (Catterall & Bewley, 1979). The mechanisms and effects of neutron irradiation differ from those of photon therapy (Hall, 1978), which has implications both for the control of tumours and for effects on normal tissues. Neutrons have been shown to be more effective in the treatment of tumours resistant to conventional photon therapy (Battermann et al, 1981; Laramore et al, 1985). However, severe fibrosis, damage to the dermis and mucous membranes, neuronal damage and osteo-radionecrosis have also been noted as late side-effects of this treatment (MRC Neutron Therapy Working Group, 1986).

Neutrons have been used by several centres in the treatment of head and neck cancer (Battermann & Mijnherr, 1986), including the MRC Cyclotron Unit at Hammersmith Hospital (Catterall & Bewley, 1979). Whilst dysphagia is a well documented sequela of treatment via surgery and photon radiotherapy (van den Bogaert et al, 1984), no systematic studies of this deficit have been carried out in patients treated with neutrons. At the Joint Dysphagia Clinic at Hammersmith Hospital, we reviewed several cured patients who developed severe dysphagia. In this paper, we report our findings in nine patients, using videofluoroscopy. This is a well established method of clinical investigation, which assists in the analysis of the complex reflex of swallowing and the decisions regarding patient management (Logemann, 1983).

Patients

Nine patients were reviewed between 1986 and 1987. Details relating to these subjects, their disease and treatment can be found in Table I.

There were nine patients (eight males and one female) ranging in age from 32 to 79 years of age. All patients presented with tumours confined to the oropharynx and were treated with similar doses and number of fractions of neutrons. Patients reported increasing difficulty with swallowing within the first 2 years following treatment.

Methods

A combined approach was adopted involving the radiologist, speech therapist and ENT surgeon. Findings were recorded on a standard form, shown in Fig. 1. A careful history was obtained, paying particular attention to the patient's description of difficulty, consistencies managed, the presence and timing of coughing and the presence of significant food residue left after the swallow (see Fig. 1).

In our examination, we differ from many reported studies in concentrating only on those aspects of sensory and motor function we consider most pertinent to the swallow itself. These are shown in the clinical examination column of Fig. 1. The method of recording is on a three-point scale from left to right, *i.e.* normal—mild impairment—gross impairment. Oral sensation is assessed by light touch, although this is fairly crude, as we have been unable to find a more useful alternative.

The modified barium swallow was then performed on all patients with video recordings involving two consistencies of contrast medium. The consistencies were liquid and milk-shake made with 50% Nesquik and 50% Baritop 100 (Concept Pharmaceuticals) and a semi-solid mousse made with 50% Angel Delight and 50% Baritop G (Concept). Solids were included for some subjects but most had indicated that they were unable to swallow solids, and therefore assessment on a full range of consistencies was not included. Small volumes were used to avoid any risk of aspiration (2–5 ml liquid to one-quarter of a small biscuit). Several swallows were recorded with each consistency in both antero-posterior (AP) and lateral views.

Each phase of the swallow was examined anatomically and functionally. The left-hand column of Fig. 1 shows the phases of a normal swallow; the next

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Table 1. Details of patients in study

Case	Sex	Age (years)	Site of tumour	Date of treatment	Fast neutron therapy	Onset of dysphagia
1	M	61	L. tonsil	1975	1560 cGy in 12 fractions over 26 days	< 2 years
2	M	36	R. tongue/vallecula	1975	1560 cGy in 15 fractions over 39 days	< 6 months
3	M	66	R. tonsil/tongue/soft palate	1978	1560 cGy in 12 fractions over 35 days	< 6 months
4	M	32	L. submandibular	1978	Surgical resection and 1560 cGy in 12 fractions over days	< 6 months (marked worsening 9 years later)
5	M	51	R. tongue/floor of mouth	1981	1648 cGy in nine fractions over 21 days	< 2 years
6	F	79	L. submandibular	1981	Surgical resection and 1483 cGy in nine fractions over days	< 6 months
7	M	70	R. tongue	1982	1599 cGy in 12 fractions over 54 days	< 2 years
8	M	68	R. tongue	1983	1560 cGy in 12 fractions over 33 days	< 2 years
9	M	57	R. tonsil/vallecula	1983	1560 cGy in 12 fractions over 35 days (+ prophylactic DXT)	< 1 year

column describes the movements involved in each phase. If an abnormality is present and produces no functional deficit, it is classified as "compensated"

(Buchholz et al, 1985) and marked "C" in the box under the appropriate consistency. The method of compensation can be recorded in the space to the right

Dysphagia clinic evaluation		HAMMERSMITH HOSPITAL		DEPARTMENTS OF SPEECH THERAPY & RADIOLOGY	
Patient's name: _____		Hosp.No. _____		Assessors: _____ Date of study: _____	
Date of birth: _____		Hosp.No. _____		☐ M ☐ F ☐ A ☐ S ☐ L ☐ N ☐ O ☐ A ☐ B ☐ C ☐ D ☐ E ☐ F ☐ G ☐ H ☐ I ☐ J ☐ K ☐ L ☐ M ☐ N ☐ O ☐ P ☐ Q ☐ R ☐ S ☐ T ☐ U ☐ V ☐ W ☐ X ☐ Y ☐ Z	
CLINICAL PROBLEM		CLINICAL EXAMINATION		VIDEOLUOROSCOPIC STUDY	
Diagnostic category (specific details) ☐ Neoplastic: histology: _____ site: _____ Date diagnosed: _____ ☐ Radiotherapy: _____ Date of operation: _____ ☐ Surgery: procedure: _____ Date diagnosed: _____ ☐ Neurological/myopathic: _____ ☐ Other: _____		LABIAL s. _____ f. Range of motion _____ Lip closure maintained _____ on jaw opening. _____ BUCCAL s. _____ JAW s. _____ f. opening/closing _____ Lateral movement _____ DENTITION s. _____ LINGUAL s. _____ f. to alveolus _____ to palate _____ protrusion _____ retraction _____ to left cheek _____ to right cheek _____ VELAR s. _____ f. elevat./retract. _____ Symmetry: _____ (Anemometer: ☐ hypo ☐ hypo) _____ REFLEXES f. Gag _____ Palatal _____ LARYNGEAL s. _____ f. voice quality _____ cough _____ throat clearing _____ INDIRECT LARYNGOSCOPY _____ RESPIRATORY s. _____ f. inhalation/exhalation _____ ORAL SENSATION _____ normal/abnormal _____		Control of oropharyngeal junction. Tongue up towards palate. ☐ ☐ ☐ Oral contrast leak into pharynx. ☐ ☐ ☐ Tongue down towards tongue. ☐ ☐ ☐ Poorly formed bolus into pharynx. ☐ ☐ ☐ Propulsion of bolus into oropharynx. Tongue up & anterior to compress bolus and strip back. ☐ ☐ ☐ Impaired/no movement into pharynx. ☐ ☐ ☐ Closure of Palato-pharyngeal isthmus. Pharyngeal palate up & back. ☐ ☐ ☐ Bolus penetration when compressed into nasal cavity. ☐ ☐ ☐ Post pharyngeal wall constrictors for'd to reach palate. ☐ ☐ ☐ Hyoid up. ☐ ☐ ☐ Initiation of reflex. ☐ ☐ ☐ Vallecula pooling/overspill. ☐ ☐ ☐ Propulsion of bolus thro. pharynx. Constrictor peristaltic wave descends. ☐ ☐ ☐ Retention in vallecula & pyriform sinuses. ☐ ☐ ☐ Protection of larynx. Tongue & hyoid move up & anterior. ☐ ☐ ☐ Penetration through larynx, before/during/after swallow. ☐ ☐ ☐ Epiglottis tilts to horizontal. ☐ ☐ ☐ Laryngeal vestibule closed. ☐ ☐ ☐ Larynx rises & closes. ☐ ☐ ☐ Pharyngo-oesophageal segment opens. Larynx moves up & anteriorly. ☐ ☐ ☐ Retention/residue of bolus +/- aspiration into larynx. ☐ ☐ ☐ Cricopharyngeus relaxes. ☐ ☐ ☐ Peristaltic wave advances. ☐ ☐ ☐ Return to rest. Palate tongue & hyoid return to rest. ☐ ☐ ☐ Larynx down & reopens. ☐ ☐ ☐ Epig. back up to vertical. ☐ ☐ ☐ Phar. oesophagus opens. ☐ ☐ ☐ Findings on PA. Asymmetry: ☐ yes ☐ no Site: _____ Pooling: ☐ yes ☐ no Site: _____ RECOMMENDATIONS _____ Signed: _____	

Figure 1. Standard form for recording patient details and study findings.

of the consistencies column. If a functional deficit occurs, this is described as "decompensated" and is marked "D" in the appropriate box. Asymmetry and pooling are noted from the AP view and recorded in the space at the bottom of the form. Oral and pharyngeal transit times can also be recorded (Logemann, 1983) and any delay in initiation of the swallow reflex noted.

Following the investigation, all the findings were discussed and recommendations made regarding future management.

Results

All nine subjects complained of worsening dysphagia of insidious onset with progressive weight loss following neutron therapy. The major complaint in all cases was that of food sticking in the throat, which was most marked with solids. For this reason, most subjects were limited to a liquid or pureed diet. Four patients complained of food/drink being lost anteriorly and three of difficulty in initiating the swallow. Five subjects reported coughing associated with swallowing; only one subject reported this as occurring frequently. Five subjects reported nasal regurgitation. Both of these latter symptoms were most marked with liquids.

On clinical examination, all patients had a characteristic appearance with localized loss of soft-tissue bulk, rigidity of the remaining tissues and telangiectasia. All had gross limitation of jaw opening and lateral movement of the jaw. Abnormalities of tongue movement varied from mild to severe impairment. The palate was generally thickened with poor mobility (Case 3 had a large, right-sided palatal defect). Two subjects had abnormalities of voice production and four reduced strength of cough, but this was rarely severe. It was difficult to test for a gag reflex because of limitations of jaw opening. However, in five cases, we were unable to elicit any gag reflex, and in one more, the gag reflex was grossly reduced. All patients complained of abnormalities of oral sensation affecting taste and tolerance of high or low temperatures. One patient (Case 4) was exceptional in showing localized neurological deficit, in that he had left-sided IX + X cranial nerve palsies with fasciculation. Neurological

opinion suggested that the most likely cause of this problem was direct involvement of these nerves by fibrosis, although pathological proof was not obtained. This patient had had prior surgical resection but this is unlikely to be implicated given the much later worsening of his dysphagia.

On videofluoroscopy, all patients presented with severe impairments of swallowing (Table II). The common areas of deficit were seen in the control of oropharyngeal junction, bolus propulsion into and through the pharynx and protection of the larynx. All subjects showed bilateral pharyngeal deficits with the exception of Case 4 who demonstrated a marked asymmetry with copious pooling in the left vallecula and pyriform sinus, but with normal clearance on the right. Delay in initiation of the reflex after the bolus had passed into the pharynx occurred in six patients and was absent (*i.e.* later than 60 s) in two. Eight of the nine patients showed aspiration varying from mild to severe. The cough reflex, however, was absent, *i.e.* laryngeal penetration occurred without eliciting an involuntary cough in six cases. Only two patients showed a deficit in closure of the palato-pharyngeal isthmus, *i.e.* movement of the bolus up into the nasopharynx. (However, small bolus size may underestimate the potential for this deficit.) In all subjects in which a swallow reflex was triggered, the cricopharyngeus appeared to relax adequately.

Attempts were made to quantify delays in triggering of the reflex and transit times through the pharynx (Table III). These observations were made using the video playback facility and a stopwatch. These measurements, although approximate, emphasize the delay in initiation of the reflex and pharyngeal transit times. (Oral transit times were not recorded and, although less impaired, were noted to be markedly delayed.)

Management

On the basis of these findings, decisions were made regarding future management. The severity of aspiration and the feasibility of compensatory/adaptive manoeuvres determined whether or not oral feeding should be continued.

Table II. Videofluoroscopy findings analysed in the consecutive stages of the swallow

Phases of swallow	Cases								
	1	2	3	4	5	6	7	8	9
Control of oropharyngeal junction	X	X	X	X	X	X	X	X	X
Propulsion of bolus into oropharynx	X	X	X			X	X	X	X
Closure of palatopharyngeal isthmus			X					X	
Initiation of reflex		D	D	D	D	D	A	D	A
Propulsion of bolus through pharynx	X	X	X	X	X	X	X	X	X
Protection of larynx	X	X		X	X	X	X	X	X
Cough reflex	A	A		A			A	A	A
Pharyngo-oesophageal segment opens									
Return to rest									

X = functional decompensation; A = absence of a reflex; D = delay in triggering of reflex.

Table III. Timing of delay in initiation of swallowing reflex following entry of bolus into pharynx and clearance of bolus through pharynx and into oesophagus

	Cases								
	1	2	3	4	5	6	7	8	9
Liquids									
Reflex initiation	2 s	8 s	4 s	25 s	10 s	2 s	A	18 s	A
Pharyngeal clearance	5 s	> 2 min	17 s	47 s	55 s	4 s	> 2 min*	> 2 min	> 2 min*
Semi-solids									
Reflex initiation	A	5 s	2 s	59 s	—	2 s	—	7 s	A
Pharyngeal clearance	> 2 min	> 2 min	58 s	> 2 min	—	5 s	—	> 2 min	> 2 min

A = absent; > 2 min = incomplete clearance after 2 min; *Aspiration of large percentage of bolus.

Recommendations were made to the referring clinicians on this basis. Accordingly, recommendations were made to transfer four patients immediately to non-oral feeding. However, this was only carried through in two cases: one with a gastrostomy, one with a pharyngostomy. The remainder continued with oral feeding with therapeutic intervention where appropriate. Therapeutic intervention included education regarding the nature of impairment, modification of consistencies included in the diet and introduction of techniques designed to minimize aspiration and pharyngeal residue (e.g. supraglottic swallow and repeat dry swallow) (Logemann, 1983).

At the 1-year review, of the two subjects for whom recommendations to transfer to non-oral feeding had not been followed, one had died with an aspiration pneumonia and the other had continued to lose weight and was thus admitted to hospital for parenteral nutrition. Of the five remaining subjects, four continued adequately on oral feeding, with one subject continuing to be closely monitored with the likely prospect of nasogastric feeding. All subjects continue to be monitored and reviewed at intervals by the Dysphagia Clinic and their weight and nutritional status monitored by the dieticians.

Discussion

In this select group of patients treated with neutrons, severe disturbances of swallowing were found, which have previously gone unreported. Although our number of subjects was small, there is a remarkable uniformity of changes in that all subjects demonstrate profound bilateral deficits in both the oral and pharyngeal phases of the swallow (whilst having apparently normal cricopharyngeal function), constant risk of aspiration and profound weight loss. The only exception to this pattern was the subject who showed focal signs of neuronal damage; the appearance on videofluoroscopy was similar to a patient with unilateral cranial nerve palsies. This subject's dysphagia was later in onset in comparison with the others.

All subjects reported progressive deterioration of swallowing. However, as these subjects were referred

several years after their treatment, we have been unable to document the natural history of these changes. To do this, serial studies from the time of treatment would be needed. Furthermore, we are only able to speculate on the pathological basis of these changes. Only one patient showed evidence of neurological damage, and in the remainder it would seem reasonable to presume that fibrosis is a major underlying cause.

Our technique of assessment has proved ideally suited for the investigation and management of these patients. Its use generally has shown that early changes can be detected and adaptive techniques instituted to prevent decompensation (Bucholz et al, 1985). The video-fluoroscopy tapes have also proved extremely useful in educating patients about the nature of their problems.

Although attempts at quantification of deficits were made, we recognize that these are crude. In future studies, use of a videorecorder with the potential for frame-by-frame analysis would facilitate more accurate timings. Whilst we were unable to carry out manometric studies, this would have been useful in confirming our observations of cricopharyngeal function in particular.

Neutrons have proven effective in disease control for head and neck cancer. However, in the patients studied, the late side-effects of therapy have compromised the functional and cosmetic results. With refinements of technique and more accurately collimated beams, these problems may diminish. The technique of investigation with the modifications we have described is ideal to assess these improvements. However, in order to determine the natural history of these changes and help patients adapt most effectively, serial studies need to be performed from the time of therapy.

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The role of computed tomography and coronal plane tomography in radiotherapy for laryngeal cancers

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Abstract. The results of a study undertaken prospectively in 1983 and 1984 to assess the value of computed tomography (CT) and conventional tomography in the planning of radiotherapy for laryngeal cancer are presented. Of 32 cases treated in 1983, 23 had both CT scans and coronal plane tomography prior to radiotherapy. At the end of 1983 these radiographs were reviewed and an assessment made of their value in treatment planning. As a result of this review it was decided that cancers of the larynx confined to the vocal cords should routinely have conventional coronal plane tomograms rather than CT scans. All other cases were to have CT scans and not tomograms. The results of following this policy in 1984 confirm that it is effective. There was no detriment to patients with early vocal cord cancers in performing coronal plane tomograms rather than CT scans. The survival at 24 months of both cohorts was 93%. In the more invasive cancers of the larynx, greater information about the extent of the disease was obtained using CT scans, and improved treatment plans resulted. When compared with a historical group, there appears to be an advantage for local control, 27.3% of the study group suffering local recurrence as opposed to 53.6% of the historical group.

At the beginning of 1983, shortly after the installation of a Picker 1200SX computed tomographic (CT) scanner in Newcastle General Hospital, a study was started to assess the role of CT in the planning of radiotherapy for cancers of the larynx.

Cancer of the larynx is staged using the TNM system (IUCC, 1982). Since its introduction, many centres have found the system consistent when comparing their results both internally and with those from other institutions (Jing, 1976). The stage of the disease as described by the TNM system correlates well with survival (Cachin et al, 1979; Dawes, 1980; Wang, 1983) and the early glottic cancers (glottic T1 N0 M0) do markedly better than the other cases.

The spread of tumours within the larynx and neck was recently correlated with the pathological findings at laryngectomy (Gerritsen et al, 1986). In six of 14 cases (43%) examined by CT, they demonstrated an increase in the stage of the local disease compared with that seen on clinical examination.

Other than clinical examination, direct laryngoscopy, chest radiography and conventional coronal plane tomograms of the larynx are usually used to determine the extent of subglottic spread prior to radiotherapy. Spread in the supraglottic region is more difficult to assess using conventional tomography.

During 1983 the policy at Newcastle General Hospital was that all cases of cancer of the larynx referred to Dr Dawes would be assessed by both conventional tomography and CT scanning. At the end of 1983 all the conventional tomograms and CT scans were reviewed and a new policy formulated for 1984, consisting of tomography for early glottic cancers and CT scans for all other cases.

Insufficient cancers of the larynx are seen in a short

period in our centre to allow a randomized trial to ascertain the value of CT in radiotherapy planning.

Materials and methods

Laryngeal cancers confined to the vocal cords are referred to as "glottic T1 N0 M0". Laryngeal cancers in this series other than glottic T1 N0 M0 cancers are referred to as "more invasive cancers". The details of the latter cases are given in Table I. In 1983 and 1984, 69 cases of cancer of the larynx were treated (32 in 1983 and 37 in 1984). The intention for the 1983 cases was that both conventional coronal plane tomography and CT of the larynx would be carried out prior to radiotherapy. This proved possible in 23 of the 32 cases, 13 patients with purely glottic T1 N0 M0 and 10 with

Table I. Distribution of more invasive laryngeal cancers

	1983	1984	Total
Supraglottis			
T1 N0 M0	2	2	4
T2 N0 M0	2	3	5
T3 N0 M0	1	3	4
T4 N0 M0	1	1	2
All T stages, N1 +	1	1	2
Glottis			
T2 N0 M0	6	9	15
T3 N0 M0	1	0	1
T4 N0 M0	0	1	1
All T stages, N1 +	1	1	2
Subglottic			
All stages	1	1	2
Total	16	22	38

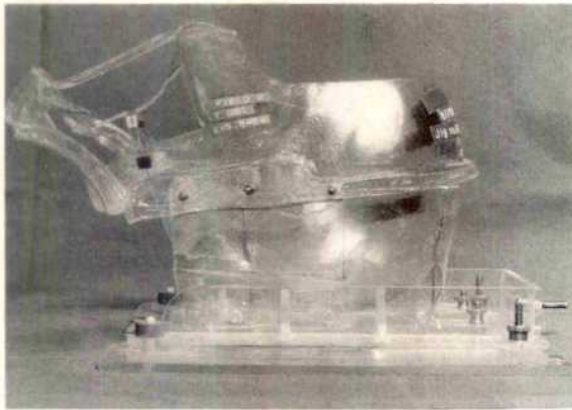


Figure 1. Treatment shell used in the radiotherapy of laryngeal cancer. The entrance and exit points of the treatment beams are carried on small strips crossing the "cut-outs".

more advanced cancers. Six cases had advanced cancer and only CT was performed because of the patients' poor general condition.

The CT scans consisted of contiguous 5 mm thick axial sections obtained during a long, slow inspiration. The first patient was scanned twice. Initially it was done with the patient lying on the CT scanner couch in the normal manner. The scan was then performed with the patient in the treatment shell to be used during the radiotherapy treatment (Fig. 1). Only one modification was made to the shell, namely that the brass nuts and bolts holding the shell together were replaced by teflon nuts and bolts. The latter do not cause streaking on the scan. There was no loss in diagnostic quality when the scan was performed in the shell and all subsequent scans were performed in the treatment shell only. The advantage of this is that the information collected by the scan is in the correct position for direct use in treatment planning.

"Minimal disease" has been used to refer to those cases where the only abnormality shown on CT or tomography was vocal cord thickening.

Of the 37 cases of carcinoma of the larynx seen in 1984, 30 were investigated in the above manner, 18 with glottic T1 N0 M0 cancers and 12 with more invasive cancers. Seven cases were not investigated according to the protocol. Of two cases of glottic T1 N0 M0 cancer, one had neither coronal tomograms nor CT because of organizational problems and the other had CT because of concern over clinical staging. Of the more invasive cancers, four patients did not have CT because they were not fit and one with early supraglottic cancer had coronal tomography in an attempt to assess subglottic spread, which had been suggested at direct laryngoscopy.

The overall distribution of the 53 cases investigated according to the protocol was 23 in 1983 and 30 in 1984. The two cohorts were followed-up for at least 24 months from treatment or until death. They were assessed regularly for local recurrence or distal spread.

Table II. Review of 1983 cases

	Tomogram +	Tomogram -	Total
T1 N0 M0 Glottic			
More extensive disease on CT than on clinical examination	0	0	0
CT findings same as clinical findings	4	9	13
Total	4	9	13
More invasive cancers			
More extensive disease on CT than on clinical examination	5	2	7
CT findings same as clinical findings	2	1	3
Total	7	3	10

The study group has been compared with an historical control group consisting of 84 patients with "more invasive" cancer treated by Dr Dawes between 1977 and 1982. The distribution of cases and radiation dose is similar between the groups. The number of cases treated with shells in both groups is comparable. The χ^2 test (with Yates' correction) was used to test the null hypothesis that the local control achieved in the two groups was no different.

Results

1983 patients

As shown in Table II, of 13 patients with glottic T1 N0 M0 cancers, CT showed minimal disease in four patients who had a positive coronal tomogram (for subglottic involvement). The CT scans did not show any extraglottic involvement.

In the more invasive cancers, CT showed extensive disease in seven and showed minimal disease in three. In two of the seven cases with extensive disease on CT, the coronal tomogram showed minimal disease. However, in two cases coronal tomography demonstrated minimal subglottic involvement not detected by CT.

In the "more invasive" cancers investigated in 1983, six of 10 cases had the treatment plan altered as a result of the CT findings. The case shown in Figs 2-4 is typical of the alterations made to the treatment plan. Four of

Table III. 1984 cases investigated to protocol

	Glottic T1 N0 M0	More invasive cancers
Tomograms confirm tumours confined to vocal cords only	13	CT = clinical assessment (7)
Tomograms show disease more extensive than vocal cords	0	CT > clinical assessment (10)

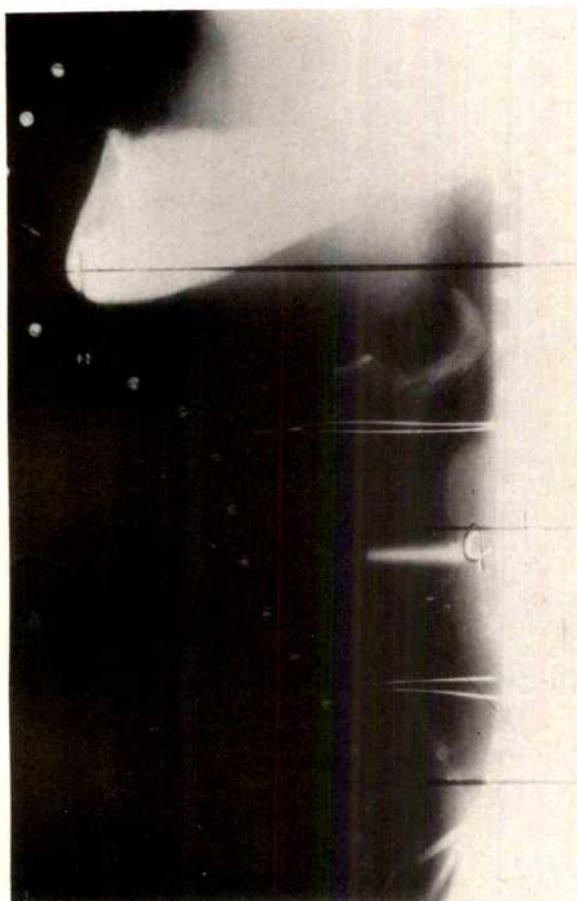


Figure 2. Lateral simulator radiograph used for tumour localization. The cranial caudal limits of the tumour are marked with fine wires.

these six patients have survived longer than 2 years without recurrence. One of these four survivors has died since from a second primary cancer (bronchogenic cancer). Two of the six patients with improved treatment plans died from their tumour, one from local failure and one from metastatic disease. The suggestion here is that CT contributed to improved survival.

The CT findings did not influence the size of the treatment fields for glottic T1 N0 M0 cancers and for this reason CT was not used to investigate these cancers in 1984.

1984 patients

Table III shows the findings of coronal plane tomography in the 13 glottic T1 N0 M0 cancers and CT in 17 "more invasive" cancers.

In the "more invasive" cancers treated in 1984, five patients with more invasive cancers did not have CT. All but one of these five patients have died from recurrent disease. The surviving patient had a local recurrence but has been salvaged by laryngectomy. A

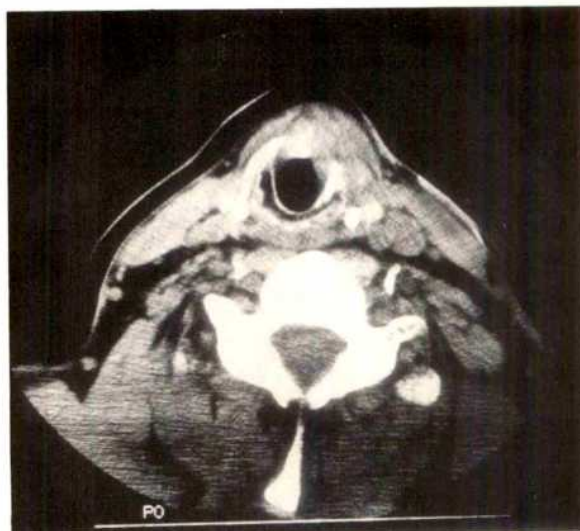


Figure 3. A CT scan taken in the treatment shell (seen overlying the skin). Tumour invasion through the cartilage is seen on the left.

patient with early supraglottic cancer was investigated by conventional tomography only and has died from nodal recurrence. One of the advanced cases, who had nodal disease at presentation, died from lung metastases. The other two who did not have CT died from local recurrence.

Of the 17 cases who were investigated by CT, five have died from local recurrence. Of those who did not recur, three patients had minimal disease detected on CT and all these are alive. In five cases, the fields were altered as a result of the CT study; four of these patients are alive and well and the other has died from a myocardial infarction with no evidence of recurrence. Four patients who were assessed by CT did not have any alteration in the plan, as the assessment agreed with

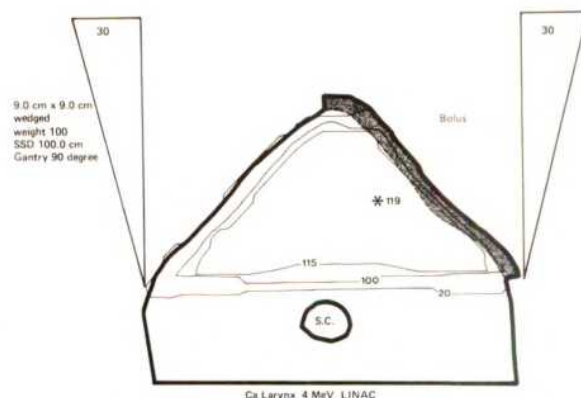


Figure 4. Treatment plan for the same patient as in Figs 2 and 3. Tissue-equivalent bolus has been placed over the skin to bring the treatment isodose (115%) to the skin surface. The patient is alive and well 46 months after treatment.

Table IV. Disease-free survival at 24 months

	1983	1984	Total
Cancers confined to vocal cords (glottic T1 N0 M0)	15/16 (93.8%)	14/15 (93.3%)	29/31 (93.5%)
More invasive cancers	11/16 (68.8%)	12/22 (54.5%)	23/38 (60.5%)
Total	26/32 (81.3%)	26/37 (70.3%)	52/69 (75.4%)

the clinical examination. These are alive and well. Of the 17 "more invasive" cancer patients treated in 1984 who had CT, five (29.4%) have recurred in 24 months.

Follow-up

The two cohorts have been followed-up till death or at least 24 months. Five patients have died from intercurrent disease without any evidence of recurrence. Of the patients with glottic T1 N0 M0 cancers, two have died from myocardial infarctions (11 and 26 months) and one from a carcinoma of the bronchus (33 months). Of the "more invasive" cancers, two patients have died from intercurrent disease, one from a myocardial infarction (7 months) and one from a carcinoma of the bronchus (29 months).

The disease-free survival at 24 months for the various groups as a result of radiotherapy is shown in Table IV. The actuarial disease-free survival is shown graphically in Fig. 5.

When the study group is compared with the historical controls, local control is defined as the absence of cancer within the irradiated volume at the time of assessment. The control group was treated between 1977 and 1982 and 45 of 84 cases (53.62%) had recurred locally by 2 years compared with nine of 31 (27.3%) CT scanned cases treated in 1983 and 1984. This difference is significant ($\chi^2 = 5.57$; $p < 0.025$).

Discussion

Pathological examination of laryngectomy specimens has shown that CT correlates well with the pathological findings, the increase in T-staging being largely due to finding cartilaginous invasion. Lateral and posterior direct spread and involved nodes are also found on occasions (Gerritson et al, 1986). Our findings confirmed this increase in the stage of the disease for tumours other than glottic T1 N0 M0 carcinomas.

The manner in which CT studies of the larynx are made does not allow adequate assessment of early subglottic spread. Owing to partial volume effects within the 5 mm slices, minimal subglottic involvement cannot be seen. Coronal plane tomograms show loss of the normal angle between the vocal cords and the tracheal wall very well. This study confirms this and shows that for glottic T1 N0 M0 cancers survival was not affected by omitting CT.

In the more invasive cancers there has been an

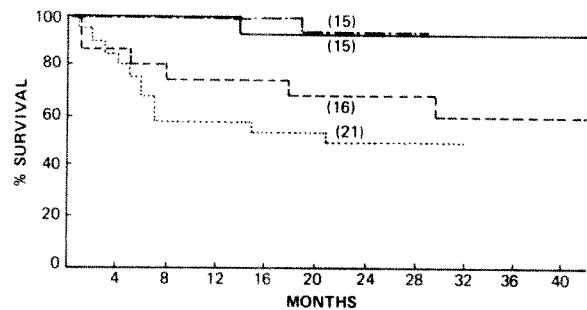


Figure 5. Disease-free survival (actuarially determined) for laryngeal cancers treated during 1983 and 1984. (—) Glottic T1 N0 M0, 1983; (---) glottic T1 N0 M0, 1984; (---) other cancers, 1983; (.....) other cancers, 1984.

improvement in the assessment of the extent of the tumour as a result of CT scanning and when compared with historical controls, local control is improved as a result of better tumour coverage by radiotherapy, after CT assessment in the treatment position. It is also notable that those cases who did not have CT scans did poorly (albeit that four of these cases had advanced disease).

Very ill patients with laryngeal cancer may find CT examination arduous but failure to assess the disease by CT was associated with complete failure to control the tumour. Despite the poor prognosis and difficulties for the patient, CT should be performed if at all possible, as improved radiotherapy is possibly the only way to improve the prognosis.

Insufficient information about lymph node involvement was generated in this study; only three patients developed metastatic neck glands after radiotherapy, and none of these patients had early cancers of the vocal cords.

As a result of this study the following policy is now adopted. Where the direct laryngoscopy shows the tumour is confined to the vocal cords and the surgeon expresses no doubt that this is the case, conventional tomograms of the larynx are routinely requested. In all other cases, CT in the treatment position is requested, even if the patient is not very fit.

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A review of occupational exposure in the North-Western Region

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Abstract. The *Ionizing Radiations Regulations 1985* require employers to monitor all classified persons and to demonstrate that all non-classified persons who work in controlled areas do not exceed three-tenths (*i.e.* the classification level) of any relevant annual dose limit. A review of occupational doses was undertaken to ascertain whether any person needed to be designated as a classified person and to demonstrate compliance with the Regulation regarding non-classified staff working in controlled areas. The occupational-dose data for 1986 were compared with data for 1981 to identify any areas where changes in workload, equipment or techniques had led to increases in whole-body or organ doses. The results demonstrate that the level of whole-body occupational dose received by the vast majority of NHS employees in the North-Western Regional Health Authority is, as expected, extremely low. However, two specific areas were identified where occupational doses are relatively high and need to be carefully monitored. The review has also led to a number of operational changes being implemented by the Approved Dosimetry Service.

The introduction of the *Ionizing Radiations Regulations 1985*, (IRR, 1985) has led to a re-assessment of the personnel monitoring services provided to the individual health authorities in the North-Western Region. Regulation 13 of the Regulations requires employers to monitor routinely all classified persons using an Approved Dosimetry Service (ADS) and to demonstrate, by personal monitoring or otherwise, that all non-classified persons who enter or work in controlled areas do not receive a radiation dose that would exceed three-tenths (*i.e.* the classification level) of any relevant annual dose limit.

A review of occupational exposure in the NHS throughout the Region was undertaken to ascertain whether any employee would need to be designated as a classified person and to be able to demonstrate compliance with Regulation 8 regarding non-classified staff working in controlled areas. The occupational-dose data for 1986 were compared with previously published data from our Region for 1981 (Hughes et al, 1983) to identify any areas where changes in workload patterns, equipment or techniques have led to increases in whole-body or individual organ doses.

The Personnel Radiation Dosimetry Service operated by the Regional Department of Medical Physics and Bioengineering based at the Christie Hospital, Manchester, routinely monitors 3000-3500 persons per year, and of the approximately 2000 who work in the NHS only 17 (0.9%) were designated as classified persons in 1986. In fact, of these 17 only four (0.2%) actually exceeded the 15 mSv whole-body classification level. The review demonstrated that the level of whole-body occupational dose received by the vast majority of NHS employees who work with ionizing radiations is, as expected, extremely low.

The data presented in this paper refer only to exposures from external radiations and do not include

personal doses resulting from internally deposited sources. It is assumed that the vast majority of occupationally exposed staff are irradiated uniformly and therefore the dose-equivalent determined from a single (film badge) monitor can be taken to represent the whole-body effective dose-equivalent (EDE). In those cases where exposure is non-uniform, *e.g.* during cardiac catheterization studies when certain organs are shielded by wearing lead rubber protective aprons, this approach may lead to an underestimation of the true whole-body EDE, but is considered to be acceptable (Gill et al, 1979; Faulkner & Harrison, 1988). Throughout this paper, the radiation quantity dose-equivalent, as measured by the film badge, has been abbreviated to dose.

Monitoring technique

The dosimeter used is the plastic NRPB/AERE badge holder (Heard & Jones, 1963; Jones & Marshall, 1964) with the Eastman Kodak Type 2 Personal Monitoring film. The dose-response characteristics for this dosimeter, its performance characteristics and its response to environmental influences are specified in the National Radiological Protection Board (NRPB) publication R103 (Marshall et al, 1980) for photon radiations and NRPB Information Services Sheet (Marshall, 1980) for β -ray dosimetry.

Calibration curves are produced by exposing films to a caesium-137 reference source at known dose levels. These are then used to convert the optical densities measured under the different filter areas of the badge holder to apparent doses and the true dose is then obtained using the formulae in the NRPB R103 document.

Owing to the relatively high sensitivity of the film to low-energy photon radiation, it is possible, when using an individual departmental control film, to assess accurately doses as low as 0.05 mSv above the

background level. Since the majority of the NHS monitored staff work in diagnostic radiology departments and are therefore exposed to low-energy photon radiations, an accurate dose can be obtained.

Results

The results have been grouped into three main occupational categories: radiotherapy (which includes both beam radiotherapy and brachytherapy), diagnostic radiology and nuclear medicine (both diagnostic and therapeutic use of unsealed radionuclides). Some staff will obviously work in more than one occupational area and they have been included in that category which best describes their major involvement.

Table I shows the annual whole-body dose distribution of NHS employees for 1986 compared with 1981. It can be seen that in 1986 more than 95% of NHS staff received less than 5 mSv per year (one-tenth of the annual dose limit) and approximately 90% received less than 1 mSv per year. The 1981 data follow a very similar dose-distribution pattern, the most marked difference being in the reduction in the number of staff receiving greater than 10 mSv per year, seven in 1986 compared with 33 in 1981.

The substantial decrease in the number of persons monitored in 1986 compared with 1981 does not indicate a significant decrease in the level of work with ionizing radiations but reflects the decision made to replace individual monitoring in most routine pathology (RIA) laboratories by systems of work, which include routine environmental and contamination monitoring using suitably sensitive monitors.

Radiotherapy

The group who do receive relatively high occupational doses, though still significantly less than the International Commission on Radiological Protection (ICRP) whole-body annual dose limit of 50 mSv, is staff involved in brachytherapy. This group is composed of the sealed-sources laboratory technicians, the radiotherapy theatre nurses and a number of nurses on brachytherapy wards whose duties include the removal of the intracavitary insertions and implants from patients. This group constitutes all of the classified persons in the Region. Classification was thought to be appropriate because they work in an environment where it might be possible for them to exceed the three-tenths classification level. In fact, as previously mentioned, only four exceeded the whole-body classification level (15 mSv) and none exceeded 20 mSv. The whole-body dose-distribution data for all the classified staff in the North-Western Regional Health Authority (NWRHA) are incorporated in Table III.

Table II shows the average annual whole-body dose received by all the different groups of staff, both classified and non-classified, involved in brachytherapy for both 1986 and 1981. The significant decrease in the two highest dose groups (the theatre nurses and the sealed-sources technicians) reflects a partial transition to remotely controlled afterloading techniques. Approxi-

Table I. Annual whole-body dose distribution in the NWRHA (1986)

Dose bands (mSv)	1986	1981
> 15	4 (0.2%)	10 (0.4%)
10 to 15	3 (0.2%)	23 (0.9%)
5 to 10	42 (2.2%)	27 (1.0%)
1 to 5	150 (7.9%)	240 (9.0%)
< 1	1698 (89.5%)	2360 (88.7%)
Total	1897	2660

Table II. Occupational doses from brachytherapy (whole-body dose-equivalent)

Occupational group	1986 average dose (mSv)	1981 average dose (mSv)
Radiotherapy theatre nurses	14.13	23.00
Sealed-sources technicians	6.15	14.80
Brachytherapy ward nurses	4.76	9.00 ^a
Physics staff	0.42	0.60
Radiotherapists	1.52	1.80

^aA review of the 1981 original data indicates that the average annual dose for brachytherapy ward nurses was approximately 9.00 mSv and this is the correct value to compare with the 1986 value of 4.76 mSv (see text).

mately 30% of all gynaecological intracavitary therapy in the Region is performed using two remote afterloading units and this has led to a decrease in the workload and amount of source handling and preparation, with a corresponding decrease in the dose received by these two groups.

In 1981 it tended to be the practice on brachytherapy wards that the more senior members of staff removed all the manually loaded brachytherapy sources from the patients. This relatively small group of experienced staff therefore received higher doses than the rest of the ward nurses, recording an annual whole-body dose in the range 10–15 mSv. In recent years it has been the practice to attempt to follow the ALARA principle and reduce individual doses; therefore more ward staff have been trained in the removal of these sources. The dose-distribution data in Table I, in particular the redistribution to the 5–10 mSv from the 10–15 mSv and above groups, demonstrates that this, together with the use of remote afterloading techniques, certainly has had the desired effect regarding individual annual doses. However, because the newly trained nurses are inevitably less experienced and therefore probably slightly slower in removing the implants, this practice will most probably lead to an increase in the collective dose (man-mSv). It should be noted that the occupational group identified in Table II as brachytherapy ward nurses represent a slightly different population to that identified by Hughes et al (1983) as ward nurses. The 1981 figure of 3.00 mSv that they

Table III. Occupational doses (whole-body dose-equivalent) in radiotherapy (1986) for all staff (classified and non-classified)

Occupational groups	Sample number	Dose bands (mSv)						Average annual dose (mSv)
		< 1	1 to 5	5 to 10	10 to 15	15 to 20	> 20	
Beam radiographers	54	54	—	—	—	—	—	0.23
Radiotherapists	36	19	15	2	—	—	—	1.53
Scientific/technical	19	12	5	2	—	—	—	1.33
Sealed-sources technicians	3	—	1 (1)	2 (2)	—	—	—	6.15
Radiotherapy theatre nurses	6	—	—	1 (1)	1 (1)	4 (4)	—	14.13
Brachytherapy nurses	74	4	38	30 (6)	2 (2)	—	—	4.76
Other nurses	171	129	42	—	—	—	—	0.68

The figures in parentheses represent the dose distribution for classified staff.

Table IV. Occupational doses (whole-body dose-equivalent) in diagnostic radiology (1986)

Occupational groups	Sample number	Dose bands (mSv)						Average annual dose (mSv)
		< 1	1 to 5	5 to 10	10 to 15	15 to 20	> 20	
Radiographers	889	876	13	—	—	—	—	0.36
Radiologists	94	82	11	1	—	—	—	0.57
Cardiologists	29	21	6	2	—	—	—	1.30
Scientific/technical	22	20	2	—	—	—	—	0.32
Departmental nurses	62	62	—	—	—	—	—	0.31
Other staff	211	211	—	—	—	—	—	0.09

quoted is the average value for all monitored ward nurses, including those who work on non-brachytherapy wards, whereas the 1986 value of 4.76 mSv represents only those identified as working on the brachytherapy wards. We have reviewed the original 1981 data in an attempt to identify the brachytherapy nurses and obtained a value for the average annual dose of approximately 9.00 mSv.

The occupational whole-body dose distribution for all staff (classified and non-classified) involved in radiotherapy, including beam radiotherapy as well as brachytherapy, is shown in Table III. Nurses on non-brachytherapy wards were monitored because of the possibility of patients undergoing treatment with unsealed radioactive sources, primarily ^{131}I for thyroid disorders, being nursed on these wards. The rotation of nursing staff through different wards during the year also led to problems in identifying those nurses for whom personal monitoring was required. Since 1986, new nursing management practices have enabled us to identify better those nurses who are occupationally exposed and therefore require monitoring.

Diagnostic radiology

The occupational whole-body dose data for this group is shown, together with the dose distribution, in Table IV. As can be seen from the final column, the average annual dose for all occupational categories is significantly less than 5 mSv, the one-tenth annual dose limit level, and in most cases is less than 1 mSv per annum. These data show that only three persons (one

radiologist and two cardiologists) received an annual whole-body dose in excess of 5 mSv and of these three, the maximum recorded whole-body dose was 6.70 mSv.

When the average whole-body dose data for 1986 is compared with that for 1981, as shown in Table V, it can be seen that the occupational-dose distribution between the various groups in diagnostic radiology has not undergone any significant change. It should be noted that in the earlier review (Hughes et al, 1983), cardiologists together with other clinicians who occasionally used X-ray screening units were included in the radiologists group. For the purposes of this review, the cardiologists were treated as a separate group and their occupational exposure will be discussed in greater detail later in this paper. The group under the heading "other staff" comprises a variety of people who

Table V. Occupational doses in diagnostic radiology

Occupational group	Whole-body dose-equivalent	
	1986 Average dose (mSv)	1981 Average dose (mSv)
Radiographers	0.36	0.37
Radiologists	0.57	0.51
Cardiologists	1.30	—
Scientific/technical	0.32	0.37
Departmental nurses	0.31	0.35
Other staff	0.09	0.18

Table VI. Occupational doses (whole-body dose-equivalent) in nuclear medicine (1986)

Occupational groups	Sample number	Dose bands (mSv)						Average annual dose (mSv)
		< 1	1 to 5	5 to 10	10 to 15	15 to 20	> 20	
Pharmacy technicians	15	12	3	—	—	—	—	0.62
Radiographers/technicians	42	26	14	2	—	—	—	1.26
Physicists	16	16	—	—	—	—	—	0.42
Clinicians	5	5	—	—	—	—	—	0.72
Research technicians	149	149	—	—	—	—	—	0.07

occasionally may enter controlled areas in diagnostic radiology departments; these include porters, dark room technicians, clerks, etc. In many departments throughout the NWRHA this group of staff is no longer monitored.

The major group of occupationally exposed persons in these departments, the diagnostic radiographers, received an average annual whole-body dose of 0.36 mSv, which is very similar to the average dose of 0.37 mSv recorded in 1981. Since this review, the monitoring period for most staff working in routine diagnostic radiology departments was extended from 4 weeks to 8 weeks. This decision was based not only on this review of occupational doses but also on experimental work to assess the performance of the film badge dosimeter, especially related to latent image fading, over longer monitoring periods. Since the introduction over 18 months ago of a longer monitoring period, we have not noticed any increase in problems associated with the use of film and feel that the assessment of our doses has improved.

Nuclear medicine

The nuclear medicine category includes data from 12 diagnostic imaging centres throughout the NWRHA and three radiopharmacy units, including the Radioisotope Department at the Christie Hospital, which also dispenses the ^{131}I for therapeutic use. The data also include staff from the research laboratories at the Christie Hospital and the associated Paterson Research Laboratories who perform mainly *in vitro* or animal *in vivo* radionuclide studies. The main radionuclides used within this group are $^{99}\text{Tc}^{\text{m}}$, ^{131}I , ^3H , ^{14}C and ^{32}P .

The whole-body dose data for nuclear medicine are shown in Table VI. The choice of appropriate categories for staff is especially difficult in this group. The pharmacy technician group includes only the technical staff of the two regional radiopharmacies at Christie Hospital and the Royal Preston Hospital. Other nuclear medicine radiographers/technicians may also dispense radiopharmaceuticals as part of their normal imaging work and they have been included with the imaging group. Some radiologists spend a few sessions in nuclear medicine departments but we have only included in the clinicians group those clinical staff who are attached to such departments either full-time or for the majority of their time. The maximum whole-body doses received by

staff in this category were by two radiographers who recorded annual doses of just over 5 mSv (5.20 mSv and 5.40 mSv). They both worked in large imaging units and also dispensed radiopharmaceuticals.

Organ/tissue doses

It is important to remember that in some cases an assessment of whole-body doses may not be the best indicator of occupational exposure. It may be necessary to monitor the radiation doses received by other organs, either routinely or for a limited trial period, in order to demonstrate that these also do not exceed three-tenths of the relevant dose limit. The lens of the eye and the extremities are examples of organs where an assessment of non-stochastic risk may be required.

One reason why extra monitoring may be necessary in certain situations, to satisfy Regulation 25 ("Assessment of Hazards") of the *Ionizing Radiations Regulations 1985*, is the increasing use of X-ray screening units with overcouch X-ray tubes or multiangular C-arm units. This leads to a change in the spatial distribution of the scattered radiation and can lead to an increase in the operators' eye dose by a significant factor. An increase in eye dose by a factor of 100 has been previously reported (Faulkner & Moores, 1982). Together with the increasing use of interventional X-ray procedures, especially the use of angioplastic techniques, the annual eye dose, as monitored by a separate dosimeter, received by some cardiologists/interventional radiologists with high workloads could be approaching the classification level.

Previous publications (Faulkner & Moores, 1982; Jeans et al, 1985) have reported workload levels that, if exceeded, would lead to an operator annual eye dose greater than the relevant classification level. However, it is obviously difficult to accept workload as the only limit since the variation in the individual's annual eye dose will depend not only on the total workload but also on variation in techniques, equipment type and X-ray tube output.

Table VII shows the 1986 average annual doses received by all cardiologists working in the Region, together with examples of three individuals who have similar, high workloads. It can be seen that for an individual the results are heavily dependent on technique. What is interesting is the variation between individuals, especially for the extremities, which must reflect technique. The eye dose for these individuals is

Table VII. Cardiologists occupational dose (1986)

Cardiologists	Whole-body DE (mSv)	Eye DE (mSv)	Extremity DE (mSv)
A	2.85	22.7	30.50
B	0.70	23.6	81.70
C	0.93	22.25	46.45
Average for all NWRHA cardiologists	1.30	7.46	24.46
Classification level (three-tenths of annual dose limit)	15	45	150

DE = dose-equivalent.

between one-tenth and three-tenths of the 150 mSv annual dose limit. Is this really a significant high dose for their type of work? In fact, these cardiologists use a ceiling-mounted eye shield which, when used correctly, decreases the dose to the eye by a significant factor, depending on the lead-equivalence of the material used. In practice we have found that a decrease of at least a factor of 2 is easily obtained. It should be noted that if this device were not used, these cardiologists would exceed the classification level and therefore be subjected to all the relevant legal requirements of a classified person.

It is important to remember that being classified does not, by itself, limit an individual's occupational dose and that the ALARA principle should always be employed to keep occupational dose low.

One advantage of the use of a ceiling-mounted eye shield compared with the use of individual protective spectacles is that it is always present and when used effectively also provides a protective shield for other staff in the area.

Discussion and conclusions

This review has demonstrated that in general the level of occupational dose in the NWRHA, with a few exceptions, is extremely low. Approximately 90% of all NHS staff in this study received an annual whole-body dose of less than 1 mSv, *i.e.* below the annual dose limit for members of the public and the average UK natural background level. This result does not appear to have varied since the previous 1981 study.

The study highlighted two areas where the volume and nature of the work could increase the level of occupational exposure to certain individuals such that they may exceed the classification level. The relatively high doses associated with brachytherapy techniques are due to the preparation, measurement and manual loading of radioactive sealed sources used in gynaecological intracavitary therapy and also to their removal on the ward after treatment has been completed. This only applies to a small group of staff involved in brachytherapy. The introduction and implementation of remotely controlled afterloading techniques will greatly reduce individual and collective doses, as has already been demonstrated when

comparing the 1986 figures with those for 1981. A number of studies have been undertaken at various centres to assess the cost effectiveness and clinical merit of remote afterloading techniques and it is hoped that, in the future, the vast majority of these patients will be treated using afterloading techniques, either manual or remotely controlled.

The second area where there is a need carefully to monitor occupational doses is in cardiology/interventional radiology where under high-workload conditions the classification level for the lens of the eye (45 mSv) could be exceeded. Whilst these interventional techniques can lead to higher occupational doses being received by certain members of staff, they do, as in coronary angioplasty, also result in immediate direct benefits for the patient. It is possible therefore that a higher level of occupational dose (below the relevant three-tenths level) can be considered to be acceptable for certain categories of work.

It is important, therefore, to perform more detailed hazard assessment and monitoring to assess the "level of risk" to these staff and to identify areas where further dose reduction methods may need to be implemented to reduce these risks.

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Clinical significance of cranial nerve deficit in the therapy of nasopharyngeal carcinoma

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Abstract. The results of radiation treatment of nasopharyngeal carcinoma (NPC) have recently been improved, but the prognosis remains relatively poor in cases with cranial nerve (CN) involvement. A total of 109 cases with histologically-proven NPC and cranial nerve involvement treated during 1979-1985 were reviewed and analysed. Definitive radiotherapy (RT) was given to patients with a high upper margin of the RT field at 2.5 cm above the base of the skull to a total dose of 70.2 Gy/39 fractions/8 weeks, with two applications of intranasopharyngeal brachytherapy. There were 37 cases (34%) in Group I (upward invasion only) and 72 cases (66%) in Group II (bidirectional invasion). Abducens, trigeminal, oculomotor and facial were the commonly involved nerves. Headache was the major symptom at diagnosis and was present in 82.6% of the patients, significantly higher than in general NPC cases ($p < 0.005$). Fifty per cent (31/62) achieved complete response to definitive RT, but it did not correlate well with survival rate. The residual neurological deficit of each CN ranged from 31 to 57%. The actuarial 5-year survival rates of Groups I and II were similar in spite of neck lymph node metastasis in Group II (33% (I) compared with 24% (II); $p > 0.05$). Cases with single CN deficit did not show better results than those with multiple CN involvements. Five-year survivors were seen only in those who received a complete course of definitive RT.

Nasopharyngeal carcinoma with cranial nerve deficit (NPC-CN) comprises 20-25% of overall NPC cases (Ho, 1978; Huang, 1980; Lynn & Hsu, 1982). It is categorized as T4 using most staging systems (Beahrs & Myers, 1983) because it represents a grave symptom and a poor prognostic sign. Clinically, it is hard to make an early diagnosis, especially in cases who present with CN deficit without an exophytic mass at the nasopharynx and/or neck lymphadenopathy. Persistent neurological deficit after definitive RT might or might not lead to poor quality of life.

We have treated definitively a selected number of patients with NPC and CN deficit. This study analysed the status of neurological involvement in NPC patients and the response to radiotherapy (RT). The onset of symptoms prior to the commencement of RT and the survival rates in different types of disease extension were compared and the correlation of residual CN deficit and survival rate reported.

Materials and methods

Patients

From March 1979 to December 1985, there were 109 cases of histologically proven squamous cell carcinoma, undifferentiated or anaplastic carcinoma of the nasopharynx (NPC) presenting with cranial nerve deficit (NPC-CN) at the time of diagnosis and at the commencement of treatment at the Department of Radiation Oncology, Chang Gung Memorial Hospital.

There were two groups of cranial nerve involvement. Group I was of the upward invasive type, where the tumour invaded the intracranial fossa without clinical

evidence of lymphadenopathy. Group II comprised the bidirectional invasive type where cranial nerve deficits and neck lymph node metastasis were observed. Group I comprised 34% (37) of cases and 66% (72 cases) were in Group II. The male to female ratio was 3.7:1 and the ages ranged from 23 to 73 years, with a median age of 49 and 46 years for Groups I and II, respectively.

Cranial nerve involvement

Neurological status was evaluated initially by a neurologist and a radiation oncologist. Computed tomography (CT), including coronal sections, was used in 89% of the cases.

The cranial nerve involvements in order of decreasing frequency were abducens 70% (76/109), trigeminal nerve 54% (59/109), oculomotor 39% (43/109) and facial nerve 25% (27/109), with others as listed in Table I. Two of the 37 patients in Group I and seven out of 72 in Group II presented with bilateral cranial nerve deficits. Twenty-two patients (20%) had single cranial nerve deficit; of these 8% (3/37) were in Group I and 26% (19/72) in Group II (Table II).

Presenting symptoms

The presenting symptoms, excluding neck lymphadenopathy and neurological signs, are shown in Table III; headache was the most common (90/109). The average period from the onset to treatment was 9 months and the median time was 7 and 9 months for Groups I and II, respectively.

Treatment

Radiotherapy commenced with a 10 MV photon beam from a Clinac-18, giving 46.8 Gy/26 fractions/5

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Table I. Frequency of involved cranial nerves in patients with nasopharyngeal carcinoma

CN	Group I (n = 37)	Group II (n = 72)	Total (n = 109) ^a
II	6 (16%)	14 (19%)	20 (18%)
III	15 (41%)	28 (39%)	43 (39%)
IV	13 (35%)	18 (25%)	31 (28%)
V	23 (62%)	36 (50%)	59 (54%)
VI	31 (84%)	45 (63%)	76 (70%)
VII	16 (43%)	21 (29%)	37 (34%)
IX	11 (30%)	16 (22%)	27 (25%)
X	9 (24%)	20 (28%)	29 (27%)
XI	0	4 (6%)	4 (4%)
XII	8 (21.6%)	22 (31%)	30 (28%)

^aNine cases presented with bilateral CN palsy, two in Group I and seven in Group II.

weeks through bilateral parallel opposing fields including the whole pharynx, base of the skull and neck lymphatics as described in a preliminary report (Chen et al, 1987). The upper margin was at least 2.5 cm above the base of the skull, to include the intracranial lesion shown on CT (Fig. 1). The RT fields were then reduced to include the nasopharynx and base of the skull, but excluding spinal cord, to make the total dose up to 70.2 Gy/39 fractions/8 weeks, while the neck lymph nodes were boosted with shrinking fields of a 9–12 MeV electron beam, up to 20–30 Gy in Group II cases. The nasopharynx and base of the skull were boosted with intracavitary applications of high-dose-rate cobalt 60 via remote afterloading, delivering 10–13 Gy at 2 cm from the source in two fractions in 1–2 weeks (Leung et al, 1987). Patients receiving RT doses of less than 50 Gy were classified as "incomplete". Palliative RT was given to patients who had distant metastasis at the commencement of RT.

Follow-up and statistical analysis

All cases were followed-up for a minimum of 2 years and a maximum of 8 years, except in four cases, which were classified as "lost to follow-up" because we did not have any information after 6 months. The median follow-up period was 41 months. Actuarial life-table methods were used for analysing the results of treatment

Table II. Single cranial nerve involvement in 109 NPC-CN patients

CN	Group I (n = 3)	Group II (n = 19)	Total (n = 22)
III	0	1	1
V	0	5	5
VI	3	10	13
VII	0	2	2
XII	0	1	1
Total (% of total no. of patients)	3 (8%)	19 (26.4%)	22 (20.1%)

Table III. Presenting symptoms^a at diagnosis of 109 NPC-CN patients

Symptoms	Group I (n = 37)	Group II (n = 72)	Total (n = 109)
Headache	35 (95%) ^b	55 (76%) ^b	90 (83%)
Epistaxis	17 (46%)	34 (49%)	51 (47%)
Bloody sputum	6 (16%)	12 (17%)	18 (17%)
Tinnitus	10 (27%)	40 (56%)	50 (46%)
Hearing impairment	16 (43%)	35 (49%)	51 (47%)
Nasal obstruction	12 (32%)	38 (53%)	50 (46%)
Onset (months)			
Range	1–30	2–35	1–35
Median	7	9	8

^aException: neck lymphadenopathy, diplopia, hoarseness, facial palsy, facial numbness, ptosis or deviated tongue.

^b*p* < 0.05; Group I vs Group II.

and the cumulative 5-year survival rate was calculated. Standard error and log rank tests were used to check *p* values. Fisher's exact test was also used to compare the statistical significance between the two different patient groups.

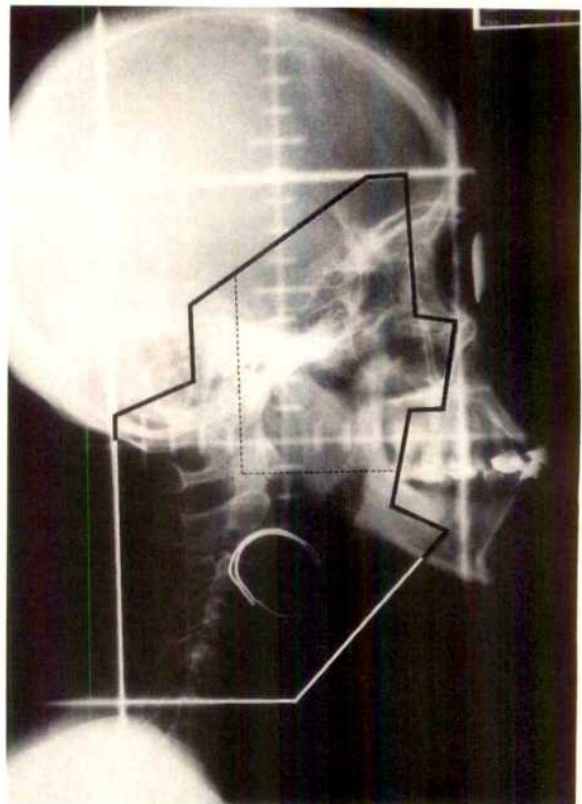


Figure 1. Radiation treatment fields for NPC-CN. The solid line indicates the initial bilateral, parallel, opposing fields for a 10 MV X-ray beam, giving 46.8 Gy/26 fractions/5 weeks. The dotted line marks the reduced fields, which exclude the spinal cord, giving a total of up to 70.2 Gy/39 fractions/8 weeks.

Table IV. Response and follow-up status of cranial nerves after definitive radiation therapy

Group	Remission of CN ^a	Relapsed CN ^b	CN control ^b	5-year survival rate
I (n = 24)	8 (33%)	2 (25%)	6 (25%)	33% } NS 24% } 28%
II (n = 38)	23 (61%)	4 (17%)	19 (50%)	
Total (n = 62)	31 (50%)	6 (20%)	25 (40%)	

^aEvaluated at 4 weeks after completion of RT. ^bEvaluated at the last visit (2–8 years after RT). NS = not significant.

Results

Survival

Table IV shows the response to radiotherapy evaluated 4 weeks after its completion, the initial remission and control rate of cranial nerve deficit and the cumulative survival rate. The control rate of CN deficit was 25% for Group I and 50% for Group II patients.

After the completion of definitive RT, gross extracranial tumour and metastatic lymph nodes regressed completely in most cases (88% in Group I and 91% in Group II). Figure 2 shows the survival curves of all 109 cases and the 62 cases that received definitive RT in Groups I and II.

Responses of the neurological deficits

The response of each cranial nerve to definitive RT is listed in Table V. The survival rates of the patients with and without residual CN deficit after definitive RT were 25 and 29%, respectively ($p > 0.05$) (Fig. 3). The actuarial 5-year survival rate of the patients in which CN signs subsided after definitive RT was slightly better than in those with a residual CN deficit but this was not statistically different. Cranial nerve remission was seen in 13 of 15 cases (87%) who had single CN deficit and definitive RT. The cumulative 5-year survival rate in this group was 38%.

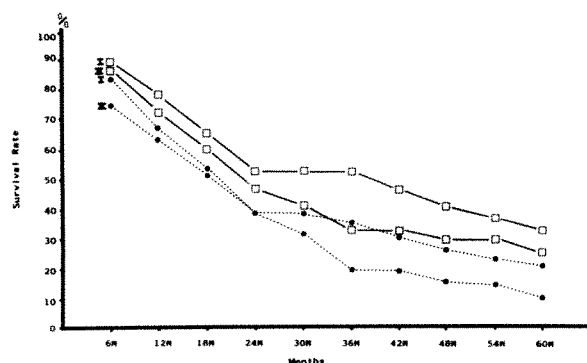


Figure 2. Actuarial survival rate of Groups I and II NPC-CN patients treated with radiation. (●...●) All cases; (□—□) cases treated with definitive RT.

The major complications of definitive RT in the 2–8 year follow-up period are listed in Table VI.

The survival curve (Fig. 2) shows that most patients died in the first 2 years, from bone, lung and liver metastasis and advanced local disease, primary or relapsed (Table VII).

Discussion

The frequency of involved cranial nerves is similar in most reports. Trigeminal and abducens nerves are the two most common involved in most series (Huang, 1980; Lynn & Hsu, 1982; Stillwagon et al, 1986). Our study showed a similar frequency of CN deficit, with the abducens the most common both in the upward and the bidirectional invasive groups (Tables I, II).

The frequency of presenting symptoms was slightly different in both groups. Headache was more common in Group I ($p < 0.05$) and was also common in NPC-CN cases overall (82.6%) compared with general NPC cases (Hsu & Tu, 1983; Unger & Chiang, 1983), although headache might be a non-specific, subjective symptom. Neck lymphadenopathy presented in Group II patients only (66.1% of our NPC-CN patients) and its incidence was lower than in general NPC cases (75–80%; $p < 0.05$) (Ho, 1978; Huang, 1980; Hsu & Tu, 1983).

Table III shows that the mean period from the onset of presenting symptoms, other than lymphadenopathy

Table V. Responses of CN after definitive radiation therapy in 62 cases

CN	No. positive		
	Before RT	After RT ^a	Residual deficit (%)
II	7	0	0
III	19	6	31
IV	12	5	42
V	38	21	55
VI	39	16	41
VII	17	8	47
IX	14	8	57
X	11	4	36
XI	1	0	0
XII	11	4	36

^aOne month after completion of definitive RT.

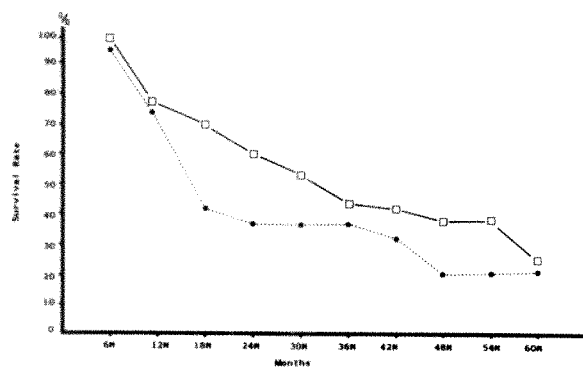


Figure 3. Actuarial survival rates of 62 patients with response to definitive radiation treatment. (□—□) No residual CN deficit; (●...●) with residual CN deficit after RT.

and cranial nerve deficits, to the commencement of RT was 7 months in Group I and 9 months in Group II. It seems that neck lymph node enlargement did not alarm the patients, which would lead to earlier diagnosis and treatment. Symptoms such as epistaxis, bloody sputum, nasal obstruction and hearing impairment were similar in both groups (Table III).

Sixty-two cases had definitive RT, 24 in Group I and 38 in Group II, and the response rate of each cranial nerve is shown in Table V. Thirty-one cases (50%), including eight in Group I and 23 in Group II, had good control for 2–8 years after RT and the other 50% had a residual or relapsed CN deficit. The frequency of residual CN deficit ranged from 31 (oculomotor) to 57% (glossopharyngeal). Stillwagon et al (1986) reported 33 to 100% complete response in different nerves. A higher remission rate of 87% (13 out of 15 cases) was seen in patients with single CN involvement but they did not have better survival compared with those with multiple CN involvements.

There is no significant difference in survival between the two groups (Table IV) in spite of neck lymph node involvement in Group II. Meanwhile, response of CN did not appear to be correlated with survival rate. Although patients with complete response of the CN may not have better survival, they regained the ability to cope with their life and daily work after improvement or

Table VI. Late complications after definitive RT for NPC with upward and bidirectional CN involvement

Complications	Upward (n = 24)	Bidirectional (n = 38)	Total (n = 62)
Xerostomia	22	35	57 (92%)
Tinnitus	15	26	41 (66%)
Hearing impairment	11	22	33 (53%)
Intractable headache	4	6	10 (16%)
Trismus	2	6	8 (13%)
Nuchal rigidity	0	7	7 (14%)
Perforation of hard palate	2	3	5 (8%)

Table VII. Causes of death^a in 47 NPC-CN cases

Failures	Group I (n = 37)	Group II (n = 72)	Total (n = 109)
(1) T and/or N	8	12	20
(2) M	4	19	23
Lung		0	6
Liver		2	8
Bone		3	16
(1) + (2)	1	3	4
Total	13	34	47

T = primary tumour; N = neck lymph node; M = distant metastasis.

^aDied before December 31, 1987.

subsidence of neurological deficits, which was a vital gain in quality of life.

The extent of tumour beyond the nasopharynx could not be properly staged using the conventional TNM system. Huang (1980), Liao and Huang (1981), Huang and Hsu (1982), Silver et al (1983) and Yamashita and Makato (1985) suggested CT, including coronal views, as an important staging method. Clinically, it was essential to determine carefully the upper margin of the RT field after proper assessment with CT, which was also indispensable for evaluation of the results.

Cranial nerve involvement has been shown in many reports to be a grave sign in NPC patients (Hoppe & Goffinet, 1976; Huang, 1980; Hsu & Tu, 1983). In our series, most patients died during the first 3 years (Figs 2, 3). With advanced intracranial invasion, local recurrence and/or distant metastasis to bone, liver or lung developed, and were fatal (Table VII). Inductive (pre-RT) and/or post-RT chemotherapy using cis-platinum and 5-fluorouracil was started recently in our hospital in a randomized prospective study in an attempt to improve further the result.

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Technical notes

A technique for total skin electron irradiation using six large flattened electron beams: implementation on linear accelerators having different modes of electron beam production

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Total skin electron beam irradiation (TSEI) has been considered for the treatment of mycosis fungoides because of the special characteristics of the electron beam, delivery of a maximum radiation dose close to the entrance surface of the tissues and a rapid fall-off in dose beyond the maximum. However, delivering a homogeneous radiation dose over all surface areas of the human body is complicated. This problem has been dealt with in various ways by different institutions.

The use of TSEI dates back to the 1950s (Lo et al, 1979) and clinical studies at Stanford University have demonstrated that TSEI may lead to a long remission or even cure if it is used in the early stages of the disease (Hoppe et al, 1979). Techniques that have been developed to irradiate the entire body surface include the use of pairs of angled beams, two to eight in number (Karzmark et al, 1960; Karzmark, 1964, 1967, 1968; Edelstein et al, 1973; Hoppe et al, 1979; Nisce et al, 1981; Coffey et al, 1982; Fraas et al, 1983; Hogstrom et al, 1984), a pendulum arc technique (Sewchand et al, 1979), and more recently, patient rotation (Kumar & Patel, 1978; Podgorsak et al, 1983).

With the use of multiple fields, the depth-dose characteristics of electron beams are changed from those of a single field because of the oblique incidence of electrons (Bjarngard et al, 1977; Pla et al, 1988). The maximum dose for a multiple-field combination is located closer to the surface with the dose falling off more rapidly beyond the maximum. These characteristics, however, are desirable for the treatment of skin malignancies. With the increase in the number of fields, the dose uniformity around the cylindrical shape of the body improves. The dose uniformity is best for the rotational techniques but is not satisfactory for a two- or four-field technique (Tetenes & Goodwin, 1977). A technique using six dual fields has been developed at Stanford University (Karzmark et al, 1960; Hoppe et al, 1979), and many institutions use variations of this technique.

A summary of techniques and requirements for dosimetry of TSEI has recently been published by the American Association of Physicists in Medicine (AAPM) in Report No. 23 (AAPM, 1988). The whole skin surface, except for areas such as the top of the head, shoulders, perineum and soles of feet, should be irradiated to a relatively homogeneous dose. Clinical practice has shown that an effective total dose is close to 40 Gy delivered in a fractionated regimen over several weeks. The penetration of the electron beam will depend on its initial energy. The electron energies considered for TSEI are in the range 3-7 MeV at the patient entrance or 4-10 MeV at the accelerator beam exit window.

At our institution, a CGR Saturne Therac 20 and a Varian Clinac 18 accelerator both produce several energies of electrons. The manner of large-field electron beam production on the Therac 20 by means of a magnetically scanned beam (Marinello et al, 1986) as compared with passing through a scattering foil is especially well suited for TSEI since undesirable photon contamination will be minimized. This accelerator was thus chosen for TSEI. However, the technique was also developed for the Clinac 18 accelerator for comparison and to serve as a back-up in our department. In order to minimize patient set-up and the complexity of vertical beam matching, a plexiglass filter was constructed, which was used to produce a large electron field encompassing the entire patient. A combination of six such large fields around the patient, one anterior, one posterior and four obliques, were used for the treatment.

Materials and methods

On the Therac 20 accelerator, the electron trimmers were not used and the collimators were opened to the maximum of 40 cm × 40 cm. This produced a radiation field size of 160 cm × 160 cm at the source-surface distance (SSD) of 400 cm with a distance of 226 cm along the diagonal. This field is large enough to encompass the average patient if the vertical height of the patient is placed along the diagonal. In order to produce a flat electron beam at the treatment distance, a plexiglass flattening filter with dimensions as shown in

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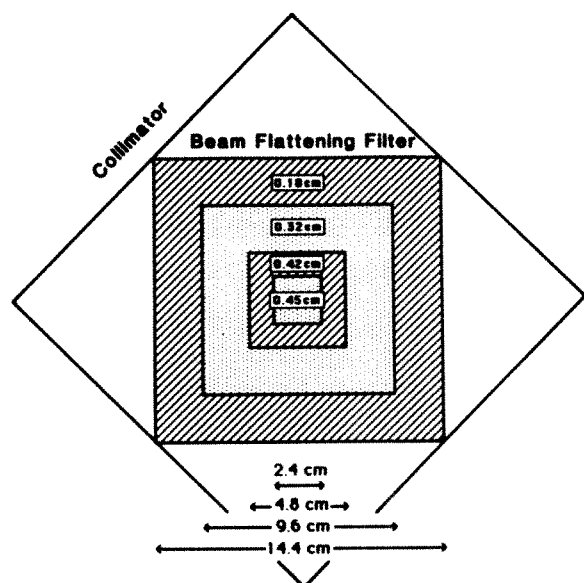


Figure 1. The position of the plexiglass flattening filter in relation to the collimator is shown. The lateral dimensions as well as the thicknesses are given.

Fig. 1 was constructed. This filter was mounted on the gantry at a distance of 48 cm from the beam exit window.

The radiation beam flatness and the percentage depth-dose for one field were measured in a plexiglass phantom for a distance of 180 cm along both diagonals of the radiation field with and without the filter in place. The measurements were performed using a parallel plate Capintec ionization chamber with associated Keithley electrometer and with thermoluminescent dosimetry (TLD-100, LiF, in powder form). For the six-field combination, the percentage depth-dose and cylindrical uniformity of the dose distribution was measured in a humanoid phantom using TLD and film dosimetry.

On the Clinac 18 accelerator the maximum collimator opening without the electron applicators was 35 cm × 35 cm. A plexiglass flattening filter was also used on this accelerator and all measurements were obtained in a similar fashion. The distance along the diagonal at 400 cm from the source was 198 cm. For patients who are taller than this, the SSD can be increased to 440 cm.

Results and discussion

Radiation beam flatness

The beam flatness measured on the surface and at 1 cm depth in a plexiglass phantom is shown in Fig. 2. The closed circles are measurements in the open field. All other points are measured with the filter in place. Circles represent values measured with the ionization chamber while the crosses represent the TLD measurements. The flatness profile was identical on the surface

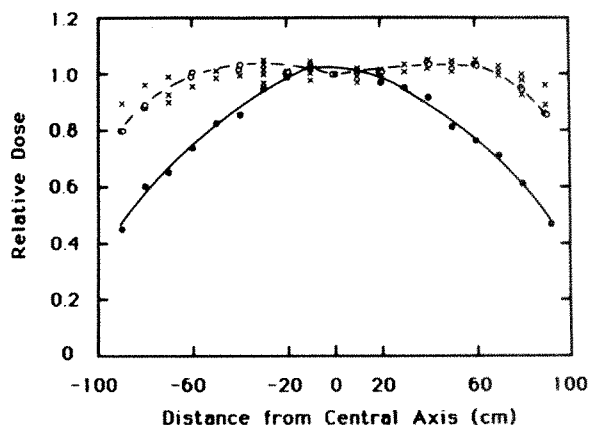


Figure 2. The variation in radiation dose with distance from the central axis at a distance of 400 cm from the beam exit window is shown. Solid circles (●) are the values measured without the filter; all other values were measured with the filter in place. (○) using an ionization chamber; (×) using TLD powder.

and at 1 cm depth in the phantom. As can be seen from Fig. 2, the beam uniformity is well within $\pm 8\%$ over a distance of 160 cm and within $\pm 4\%$ over a distance of 60 cm, and therefore satisfies the recommendations of the AAPM Report 23 (AAPM, 1988) for beam

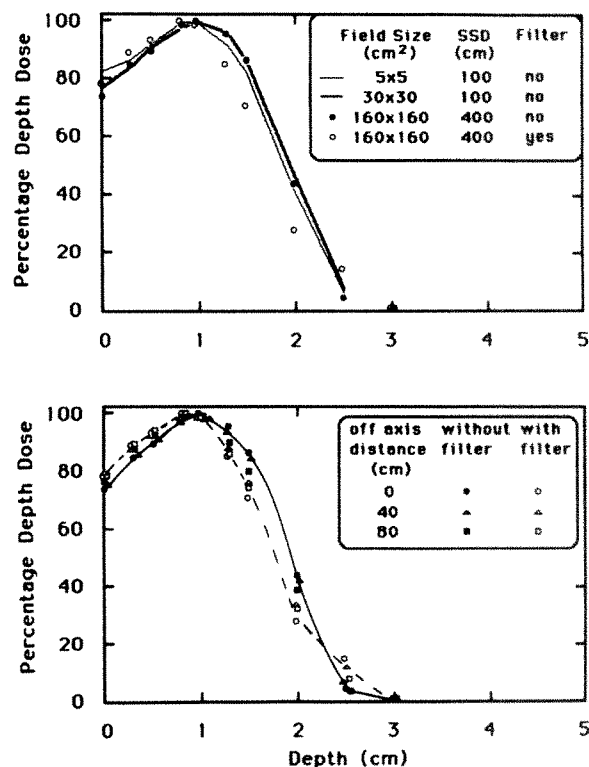


Figure 3. The variation of the percentage depth-dose with radiation field size, SSD and position of filter.

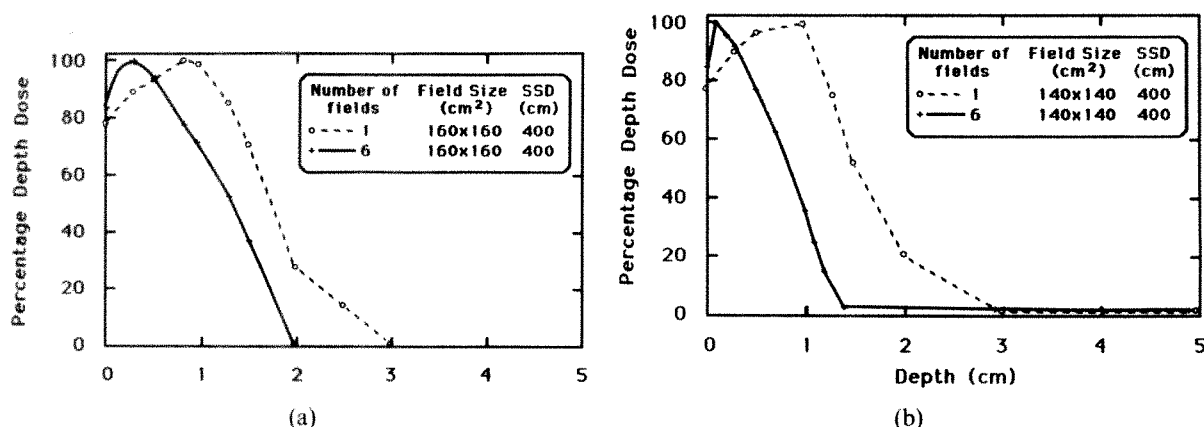


Figure 4. The percentage depth-dose in a phantom using a six-field combination is compared with a single-field irradiation at the same SSD and for the same field size for (a) the Therac 20 linear accelerator and (b) the Clinac 18 linear accelerator.

uniformity. The flattening filter for the Clinac 18 accelerator was constructed so as to obtain the field uniformity within those same limits.

Percentage depth-dose: one single field

On the Therac 20 the percentage depth-doses (PDD) for the large field with and without the filter are shown in the upper part of Fig. 3. These PDDs are compared with the PDDs for the standard fields at SSD=100 cm. The PDDs measured without the filter are similar. No change with SSD and field size after 30 cm × 30 cm is noted. However, with the filter in place (open circles) the dose is higher in the build-up region and falls off more rapidly beyond the dose maximum. For all cases, there is no measurable dose beyond a depth of 3 cm in the phantom. This means that the X-ray contamination of the beam is non-detectable beyond 3 cm as expected for the Therac 20. This result satisfies the condition of the AAPM (AAPM, 1988) that total X-ray contamination should be below 1% for TSEI treatments. On the Clinac 18 accelerator, the PDDs were modified in the same way by the flattening filter. However, there was a 1–1.5% X-ray contamination of the beam beyond a 3 cm depth.

The change in PDD with distance from the central axis was also investigated with and without the filter in place and is shown in the lower part of Fig. 3. No significant change in PDD with distance from the central axis was observed although the filter changed the PDD as discussed previously.

Percentage depth-dose: six-field combination

The PDD for a six-field combination will not be the same as that for a single field because the oblique incidence and scattering of electrons near the surface will shift the dose maximum towards the surface (Pla et al, 1988). This is a desirable effect for the treatment of skin lesions. For the six-field combination, the dose distribution was measured using TLD and film dosimetry in several slices of a humanoid phantom. The TLDs were placed on the surface, at 1 cm depth and at

2 cm depth at 3–5 cm intervals all around the slices. The phantom was then irradiated with the six fields with an equal dose delivered by each field. Film was also placed between the slices of the phantom and another six-field irradiation was done.

The PDD for the six-field combination compared with the PDD for a single field is shown in Fig. 4a for the Therac 20 accelerator and in Fig. 4b for the Clinac 18 accelerator. The dose maximum is shifted towards the surface and the dose falls off much more rapidly than that for the single field as reported previously (AAPM, 1988). For the Clinac 18, the PDD has a steeper fall-off in dose beyond the maximum both for the single field and for the six-field combination. The dose uniformity around all slices was within $\pm 8\%$.

Absolute dosimetry and patient set-up

For patient treatment, the 6 MeV electron beam produced by the Therac 20 is used with a dose-rate set at 400 MU/min. The maximum field size without the use of the electron trimmers is used. The absolute dose calibration for the six-field combination was done using TLD measurements on the surface of the humanoid phantom at SSD=400 cm. These were calibrated in a single beam both at SSD=100 cm and at SSD=400 cm using the Farmer Baldwin ionization chamber (cylindrical volume 0.6 cm³) with a Keithley electrometer according to the Hospital Physicists' Association (HPA) dosimetry protocol (HPA, 1971, 1975). Both the TLD and the ionization chamber were placed at 1 cm depth in a polystyrene phantom. The average energy of the electron beam at that point was calculated from the depth ionization curve using:

$$E_0 \text{ (MeV)} = (R_p \text{ (cm)} + 0.376) / 0.521 \text{ and} \\ E_d = E_0 (1 - d/R_p)$$

where E_d is the average energy of the electron beam at depth d , E_0 is the energy of the incident beam and R_p is the practical range of the beam. The energy of the single

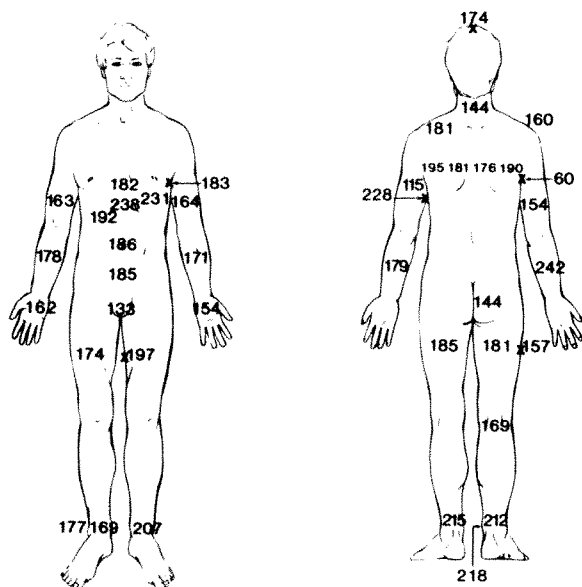


Figure 5. Radiation dose measurements using TLD powder placed on the surface of a patient treated with TSEI on the Therac 20 linear accelerator are shown in the anterior and posterior position. All doses are normalized to a 200 cGy given dose.

beam was 3.7 MeV at 1 cm depth in the phantom, which was similar to the energy of 3.8 MeV calculated at 3 mm depth for the six-field combination. The dose maximum was near the surface for the six-field combination and therefore the dose prescription was to this point. The anterior and left and right posterior oblique fields were treated on one day. The posterior and left and right anterior oblique fields were treated the following day so that a total dose of 200 cGy was delivered in 2 days. The treatment time was approximately 5 min per field. The patient was treated 4 days a week up to a total dose of 36 Gy in 9 weeks.

The patient was positioned along the beam diagonal standing on a platform at a distance of 400 cm from radiation source to patient surface. The position of the feet was painted onto the platform and the position of the arms was adjusted as in the Stanford technique (Karzmark et al, 1960) so as to reproduce patient position and to minimize self-shielding by body parts. Eyes, fingernails and toenails can be shielded. *In vivo* dosimetry should be performed using TLD. Special care must be taken to calibrate the TLDs in the same radiation beam and with the same energy, i.e. 6 MeV electrons, because the TLDs exhibit a beam energy dependence that may produce errors in dosimetry of the order of 10–15% (Holt et al, 1975). The TLDs should be placed on the patient midline and at several other positions around the patient. The TLDs should especially be placed in areas where underdosage will be expected, so that the amount of a required radiation boost can be determined. The TLD placement and

measurements on a patient are shown in Fig. 5. The doses are normalized to a dose of 200 cGy. These measurements show that a good dose uniformity can be achieved with our technique.

Conclusions

A six-field technique for total skin irradiation using a CGR Saturne Therac 20 accelerator has been developed and compared with an identical technique on a Varian Clinac 18 accelerator. By use of a plexiglass filter mounted on the treatment head, the 6 MeV electron beam was flattened so as to deliver a uniform radiation dose over a 160 cm × 160 cm field at a distance of 400 cm from the source. A six-field treatment gives a uniform dose distribution around the patient with no measurable X-ray contamination of the beam beyond a 3 cm depth.

Acknowledgments

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A simple technique for intraluminal irradiation in oesophageal tumours using the high-dose-rate Microselectron

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The majority of oesophageal cancers present at an incurable stage and any treatment is aimed at relieving unpleasant symptoms, the most important of which is dysphagia. Unless this is satisfactorily relieved, the demise of the patient is usually rapid with marked weight loss and gross wasting. Unpleasant terminal events ensue as the patient finally cannot even swallow his own saliva. Palliative external-beam radiotherapy has been used with limited success but the established methods of relieving the obstruction include repeated dilatation and the insertion of specially designed tubes at oesophagoscopy (e.g. Mousseau-Barbin or Celestin tubes). Recently, laser treatment has been used with benefit. None of these methods are ideal for palliation as they usually require hospital admission and often repeated oesophagoscopy, and may be associated with major morbidity. An easy method of palliating these patients has been eagerly awaited.

Intraluminal therapy has been used in the past to treat these patients with some success. Previous techniques have involved manual insertion of pre-loaded radioactive sources with the consequent problem of radiation protection for the staff involved. Recently, remote afterloading techniques have been employed

using the low-dose-rate Selectron (Rowland & Pagliero, 1985). This method involves inserting a relatively rigid applicator, 8 mm in diameter, whilst the patient is sedated or anaesthetized and treatment times are in the order of 90 min.

A high-dose-rate Microselectron has been under clinical evaluation at the Christie Hospital and Holt Radium Institute since April 1988. This remote afterloading machine uses a single 370 GBq (10 Ci) iridium source of 1.1 mm external diameter. Consequently, the applicator may be much narrower and treatment times much shorter. To date, 25 patients have been successfully treated without major technical problems using a simplified technique, which is described in this paper.

Technique

The oesophageal applicator, 6 mm in diameter, supplied by the manufacturer (Fig. 1) for use with the high-dose-rate Microselectron requires oesophagoscopy for insertion and the placement of a guide wire through the tumour over which the applicator is threaded. In order to overcome the need for repeated oesophagoscopy, we have used a standard Microselectron bronchial applicator, 1.9 mm external diameter, which is placed within a 14-gauge nasogastric tube (Fig. 2) to facilitate swallowing and to reduce movement inside the oesophagus. The nasogastric tube also prevents kinking

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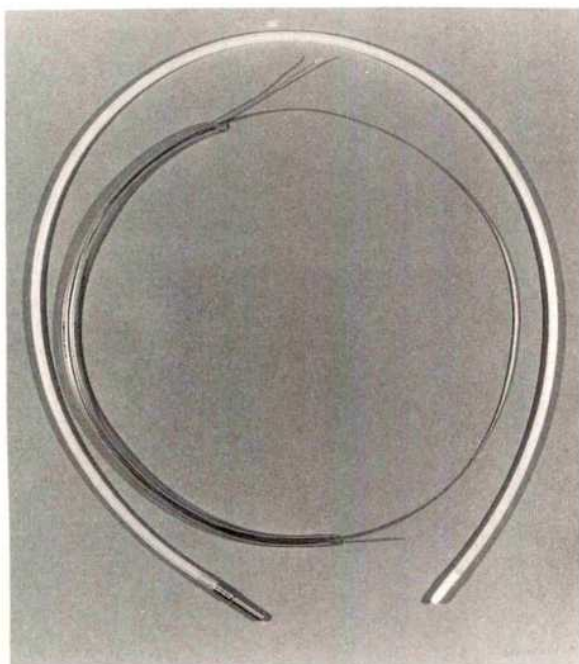


Figure 1. Standard high-dose-rate Microselectron applicator with guide wire.

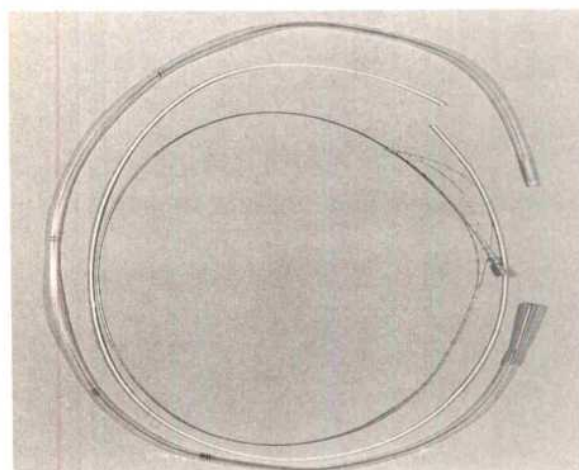


Figure 2. Manchester apparatus showing (from the outside): the 14-gauge nasogastric tube, standard Microselectron bronchial applicator and radiographic wire insert.

As the radiographic insert is graduated in 1 cm intervals, corresponding to the dwell positions of the source inside the applicator, a loading pattern can then be chosen to treat the affected length of oesophagus with a generous margin at either end, remembering the

of the applicator and protects tissue from a very high dose of radiation on the surface of the applicator.

The correct degree of flexibility is achieved if the tube is deep-frozen before use. Since the nasogastric tubes are longer than the bronchial applicator, the proximal 15 cm of the tube are cut off. The bronchial applicator is coated with the lubricating jelly and is inserted into the nasogastric tube leaving no dead space, before insertion into the patient.

A lignocaine local anaesthetic spray is used to anaesthetize the nose and nasopharynx. The nasogastric tube containing the applicator is passed in the normal way, with the patient simply having to swallow repeatedly. Once the distal end of the tube is thought to be in the stomach, the end of the tube protruding from the nostril is lightly but firmly taped to the nostril. A radiographic wire marker graduated at 1 cm intervals is inserted into the bronchial applicator and advanced as far as the tip. Antero-posterior (AP) and lateral radiographs are then taken. If the position is unsatisfactory for any reason, then adjustments can be made. The patient is asked to swallow some radio-opaque contrast medium and then a further AP radiograph is performed to outline the tumour relative to the applicator and the radiographic marker (Fig. 3). Standard diagnostic barium swallow radiographs and the findings at oesophagoscopy can be referred to at this stage to aid orientation, but identification of the tumour extent is usually possible from this one contrast medium swallow.

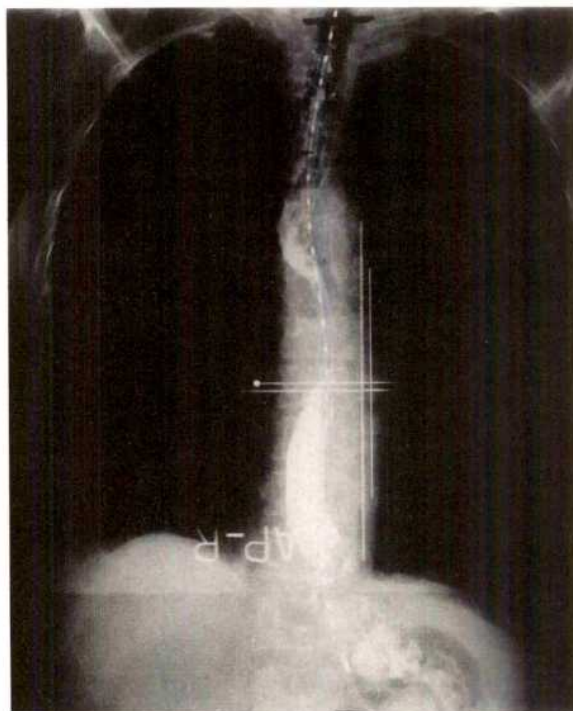


Figure 3. Check AP radiograph showing position of the nasogastric tube, bronchial applicator and radiographic wire insert in relation to tumour, which has been outlined by radiographic contrast medium.

tendency of oesophageal tumours to spread sub-mucosally. The treatment length usually chosen is between 10 and 20 cm long but can be up to 27 cm. The distal length of applicator that can be left unloaded varies according to the position of the tumour relative to the applicator. If, for example, the distal 7 cm are to be left unloaded, then a treatment length of only 20 cm is possible. If the length of oesophagus treated was to be extended proximally, it would be necessary to withdraw the nasogastric tube a few centimetres. The patient is then moved to the treatment suite and the radiographic marker removed, care being taken not to move the applicator. The bronchial applicator is then connected in the usual way to the source safe. A dose of 15 Gy (1500 cGy) expressed 1.0 cm from the centre of the applicator is most commonly used. At the end of the treatment the applicator is removed and the patient is allowed home, being warned not to drink until after the local anaesthetic has worn off. The patient is usually at the hospital for a stay of about 2 h.

Preliminary observations

All patients treated so far have tolerated the procedure extremely well with no serious morbidity. In

about 10% of patients it has not been possible to pass a nasogastric tube in this manner and these patients required oesophagoscopy with insertion of a guide wire and standard oesophageal applicator.

Conclusion

The technique presented is a novel and simple method of using the high-dose-rate Microselectron to administer palliative irradiation to oesophageal tumours using a modified applicator.

Acknowledgments

The assistance of Nucletron Trading Ltd in developing this technique is appreciated. The patience and help of our colleagues in the radiotherapy, medical physics, radium theatre and diagnostic radiography departments at the Christie Hospital is appreciated.

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Echocardiographic diagnosis of massive pulmonary embolism

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(Received January 1989 and in revised form March 1989)

The radiological diagnosis of pulmonary embolus usually involves radionuclide ventilation-perfusion scans and pulmonary angiography (Windebank, 1987). The latter is an invasive technique with inherent risks to the patient, but is recognized as the investigation of choice for visualizing the embolus in the pulmonary artery (Alderson & Martin, 1987). We report on a case of an acute, haemodynamically significant pulmonary embolism, where echocardiography provided the diagnosis and demonstrated the embolus lying in the pulmonary artery.

Case report

This patient, a 52-year-old, unmarried, domestic assistant, was admitted for investigation of 5 months amenorrhoea followed by 2 weeks of heavy vaginal bleeding. On examination, she had a large mass arising out of the pelvis, which ultrasound examination revealed to be a huge fibroid uterus. She was anaemic with a haemoglobin of 5.9 g/dl. She was commenced on norethisterone (5 mg three times daily) and transfused with 6 units of blood prior to planned hysterectomy the following week.

After 4 days, she presented with acute swelling of her left leg and gradual increase in breathlessness. She had no chest pain. Examination revealed cyanosis, a pulse rate of 80/min and a

blood pressure of 140/80 mmHg with 10 mmHg of paradox. There was a markedly raised jugular venous pressure and a palpable liver edge. The haemoglobin was 11.1 g/dl and clotting studies were normal. The postero-anterior chest radiograph showed that the heart size had increased since previous radiographs and the main pulmonary artery had become prominent. No lung abnormality was shown. A confident clinical diagnosis of deep venous thrombosis was made and heparin therapy commenced. An echocardiogram was then performed in order to assess the changing cardiac status. This showed the following features.

- (1) A lobulated mass in the inferior vena cava arising from the region behind the fibroid (Fig. 1).



Figure 1. Longitudinal view of the inferior vena cava showing thrombus (arrows) at the level of the inferior margin of the liver.

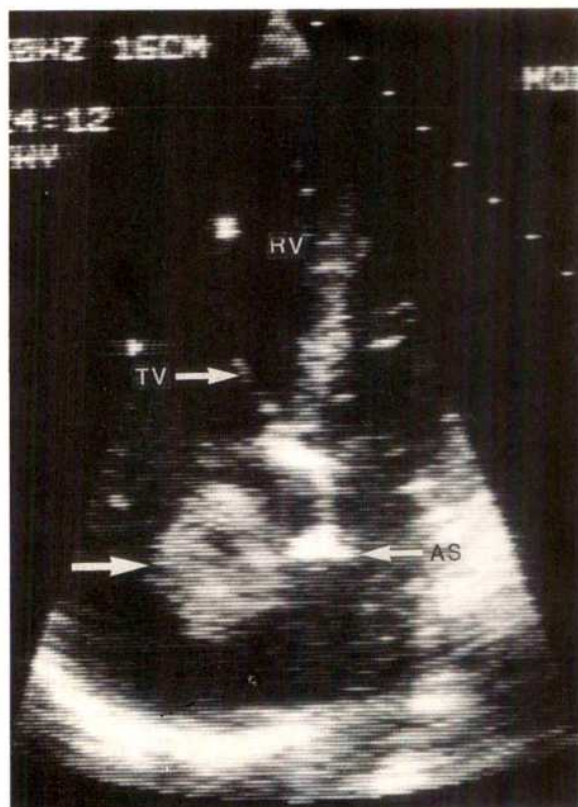


Figure 2. Apical four-chamber view showing thrombus in the right atrium (large arrow). RV=right ventricle; TV=tricuspid valve; AS=atrial septum.



Figure 3. Short-axis view through the aortic root showing thrombus (arrows) within the main pulmonary artery. RCA = right coronary artery; PA = pulmonary artery; RPA = right pulmonary artery; LPA = left pulmonary artery.

- (2) A large, mobile, pedunculated mass in the right atrium adherent to the atrial septum (Fig. 2).
- (3) A further lobulated mass in the main pulmonary artery near the origin of the right pulmonary artery. This was seen to be mobile in the vessel (Fig. 3).
- (4) A large right ventricle with moderate tricuspid regurgitation. There was evidence of moderate pulmonary hypertension, calculated by finding the pressure gradient across the tricuspid valve during regurgitation using continuous-wave Doppler techniques.



Figure 4. Post-mortem specimen of the fibroid uterus.



Figure 5. Post-mortem specimen of the lungs showing thrombus in the pulmonary arteries.

The final diagnosis was thus considered to be one of pelvic venous thrombosis secondary to compression by a fibroid uterus, leading to embolus in the pulmonary arteries and right atrium. The case was discussed with cardiac surgeons who considered that full diagnostic information had been obtained without recourse to angiography, but surgical intervention was not considered appropriate because of the widespread sites of clot. Inferior vena cava filtration was inappropriate because of the presence of thrombus in the right atrium.

The patient was started on high-dose intravenous streptokinase. Four hours later, she suffered a cardiac arrest from which she could not be resuscitated.

Post-mortem examination confirmed a large, benign, fibroid uterus (Fig. 4) and also thrombosis of the left iliac vein with embolus in the right atrium, the main pulmonary trunk and right and left pulmonary arteries (Fig. 5).

Discussion

This case shows that good-quality echocardiograms of thrombus in the right heart and pulmonary artery are possible. This examination may be adequate to diagnose pulmonary embolism with certainty.

There have been previous reports on echocardiography and pulmonary embolus. Kasper et al (1986) measured various parameters such as dilatation of the right ventricle and right pulmonary artery and reduced left ventricular cavity dimension. In his 105 patients with proven pulmonary emboli, right-sided thrombi were seen in 13 patients. In 11 patients, thrombus was in the right pulmonary artery and in three patients it was in the right ventricle, but only in one were both right heart and pulmonary thrombi seen. Farfel et al (1987) felt that two-dimensional echocardiography should precede any invasive diagnostic technique that could mobilize an entrapped thromboembolus. They also found that patients with right heart embolus-in-transit had a 50% mortality if treated by medical measures alone, whereas surgical mortality in this situation was 15%. Gray et al (1988), however, state in their review of patients with acute,

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massive, pulmonary embolism that the case for the urgent use of thrombolytic agents is powerful.

We feel that in any hospital with two-dimensional echocardiography available, this should be carried out urgently prior to pulmonary angiography in suspected cases of major pulmonary embolism. This can speed the diagnosis and may eliminate the need for angiography.

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Aneurysm of the inferior pancreaticoduodenal artery diagnosed by real-time ultrasound and pulsed Doppler

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Aneurysms of the superior mesenteric artery are rare, being noted in only 1 of 12 000 autopsies (Lucke & Rae, 1921). Aneurysms of branch arteries are even less common. Presentation is most commonly at the time of rupture, which often results in catastrophic and usually fatal haemorrhage. The incidental finding of such aneurysms and their recognition thus assumes an importance out of proportion to their frequency. A case is presented in which an incidental finding of an asymptomatic aneurysm of the inferior pancreaticoduodenal artery was made by ultrasound and pulsed Doppler. The diagnosis and exact anatomy was confirmed by angiography.

Case report

A 50-year-old woman presented to a gynaecologist complaining of vaginal bleeding and was referred for ultrasound examination of the pelvis. The patient was a normotensive non-smoker and, on direct questioning, revealed no symptoms referable to the gastrointestinal tract or upper abdomen.

The ultrasound examination revealed a 23 mm diameter sonoluculent mass in the upper abdomen immediately anterior to the aorta (Fig. 1). The mass was pulsatile and lay postero-medial to the superior mesenteric artery but appeared to communicate with it. Pulsed Doppler revealed pulsatile but turbulent arterial flow within the mass and reliably excluded pancreatic or mesenteric cyst (Fig. 2). A saccular aneurysm of the superior mesenteric artery was diagnosed and angiography was performed.

Angiography revealed a previously unsuspected stenosis of the coeliac axis (Fig. 3). The vessel distal to the stenosis was of normal calibre. The superior mesenteric artery was normal but there was aneurysmal dilatation of its first branch, the inferior pancreaticoduodenal artery, which provided a collateral blood supply to the post-stenotic coeliac axis (Fig. 4).

Discussion

Visceral aneurysms are usually asymptomatic until rapid enlargement or rupture occurs (Ugolotti et al,



Figure 1. Longitudinal scan showing an echolucent mass lying between the abdominal aorta posteriorly and the superior mesenteric artery anteriorly.

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Figure 2. Transverse scan just below the origin of the superior mesenteric artery showing a mass communicating with the artery's lumen. The Doppler tracing below, taken from the site of the cursor, shows turbulent pulsatile flow.

1984). Up to 80% of reported cases presented at the time of rupture (West et al, 1968). In a review of cases of pancreaticoduodenal artery aneurysm, 13 of the 23 patients died at or soon after the onset of presenting



Figure 3. Lateral digital subtraction aortogram showing stenosis at the origin of the coeliac axis (arrow). The origin of the superior mesenteric artery is normal but a contrast-medium-filled aneurysm is seen overlying the artery more distally.

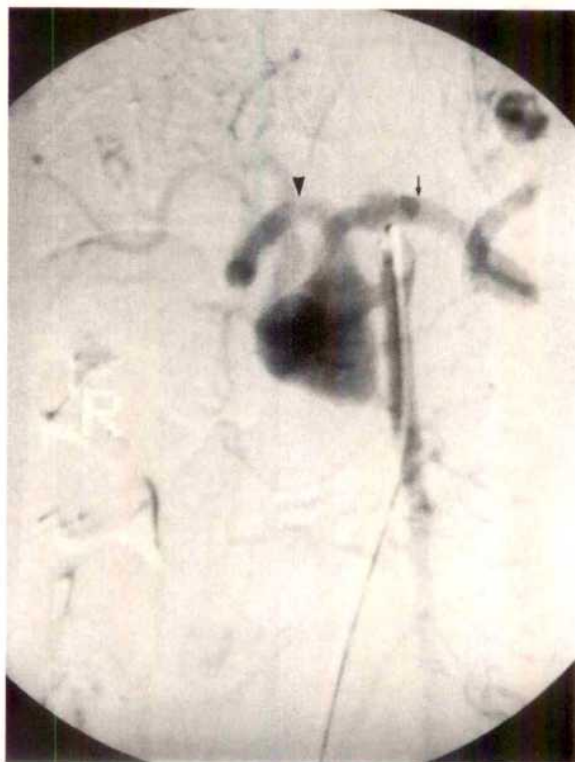


Figure 4. Selective superior mesenteric arteriogram showing an aneurysm arising just distal to the origin of the enlarged inferior pancreaticoduodenal artery. Contrast medium enters the common hepatic artery (arrowhead) and splenic artery (arrow) via the aneurysm.

symptoms. Rupture is usually retroperitoneal or intraperitoneal rather than into the gastrointestinal tract (Verta et al, 1976).

The prognosis of asymptomatic superior mesenteric branch aneurysms is unknown. Size does not appear to predict the risk of rupture and previous authors have suggested that elective resection should be undertaken (McNamara & Griska, 1980). The combination of arteriographic findings in our patient appears to be without precedent in the literature and a decision regarding future management is yet to be made.

In general, aneurysms of branches of the superior mesenteric artery can be treated by resection without restoration of continuity. This is clearly not an option in this case as the majority of blood supply to the coeliac territory is derived from the superior mesenteric artery through the aneurysmal inferior pancreaticoduodenal artery. Resection of the aneurysm with restoration of continuity is possible but the consequences of surgical mishap would be severe in this asymptomatic patient. Surgical reconstruction of the coeliac stenosis with resection of the aneurysm is surgically more demanding but may reduce this risk. A possible option would be percutaneous balloon angioplasty of the coeliac stenosis

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with resection of the aneurysm on a later occasion. Whether angioplasty of the stenosis alone would halt or cause regression of the aneurysm by reducing the flow through it is unknown.

Mycotic aneurysms account for 60% of aneurysms of the visceral arteries. A further 25% are attributed to atherosclerosis. Trauma, polyarteritis nodosa, fibromuscular dysplasia, syphilis and pancreatitis account for the remainder (Ugolotti et al, 1984). In the case presented, there was no evidence of septic emboli or of arteriosclerotic disease elsewhere. The aneurysm may have arisen as a result of increased flow through the inferior pancreaticoduodenal artery caused by the coeliac axis stenosis. The cause of the stenosis is unclear. The patient has no risk factors for arteriosclerotic disease and there was no evidence of atheroma elsewhere on the arteriogram. There was no clinical evidence of arteritis. Encasement of vessels by tumour may result in a smooth constriction of similar appearance to this case but there is no evidence of local tumour in this patient. Chronic pancreatitis, too, may result in stricturing of adjacent vessels but again there was no evidence of such pathology.

Fibromuscular hyperplasia has several histological variants with corresponding arteriographic appearances. An appearance similar to the case presented may occur in medial hyperplasia or the rarer intimal fibroplasia and periarterial fibroplasia (Abrams, 1983). Although there is no evidence of fibromuscular hyperplasia elsewhere, the authors consider this to be the most likely cause of the stenosis in this case.

The ultrasonographic appearances of visceral artery aneurysm and its confirmation by pulsed Doppler should help to distinguish these masses from pancreatic or mesenteric cysts, which may initially appear similar. Confusion has arisen in the past when lack of visible

pulsation in a mass seen on real-time scanning has resulted in unnecessary delay of diagnosis or diagnostic puncture of a visceral artery aneurysm (Ugolotti et al, 1984; Mourad et al, 1987). It appears that the lack of visible pulsation does not reliably exclude an aneurysm in this situation. The diagnosis of visceral artery aneurysm should be considered on finding a non-pulsatile cystic mass on ultrasound and arterial blood flow excluded by Doppler if facilities are available.

Acknowledgments

We wish to thank Miss A. O. Mansfield, Consultant Surgeon, for permission to report this case.

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Atlanto-axial rotary fixation: diagnosis by functional computed tomography

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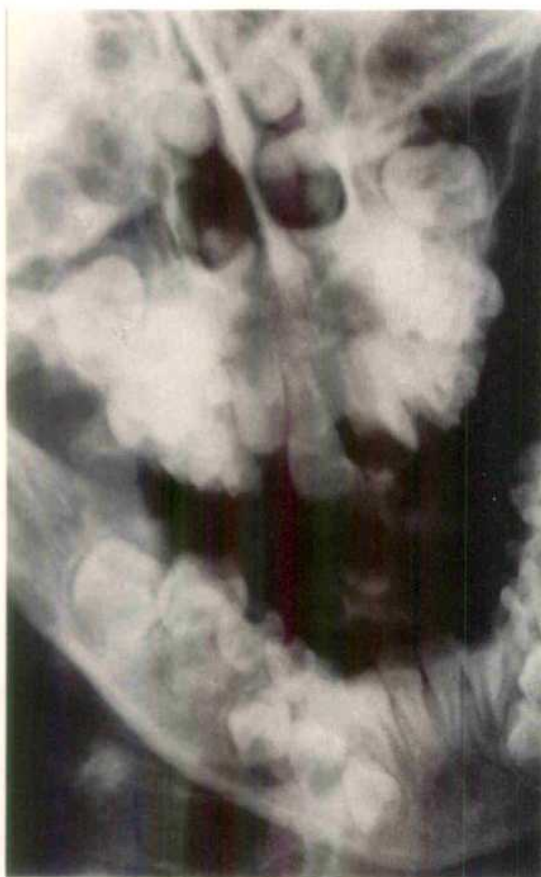
The term atlanto-axial rotary fixation was first coined in 1968 (Wortzman & Dewar, 1968). It is an unusual condition, which refers to fixation of the atlas on the axis usually within the normal range of atlanto-axial rotation. The diagnosis can be difficult to make on plain radiography and many cases present late only to require open surgery (Fielding & Hawkins, 1977). Recently,

functional computed tomography (CT) has been successfully used in a patient with atlanto-axial rotary fixation (Kowalski et al, 1987) and we discuss its value in our patient.

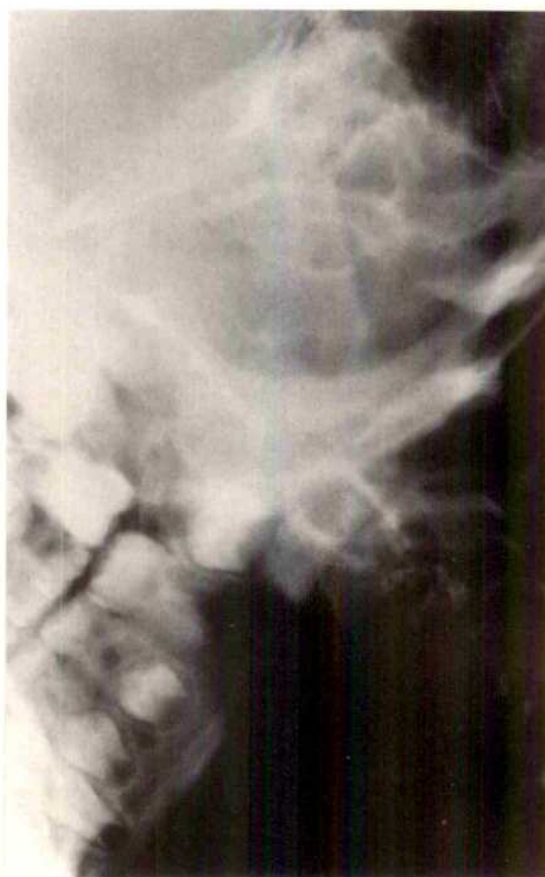
Case report

A 7-year-old girl presented with a painful torticollis of 3 weeks' duration following adenoidectomy and left myringotomy. She had a past history of neonatal *Escherichia coli* septicaemia and meningitis complicated by an intraventricular haemorrhage and subsequent arrested hydro-

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(a)



(b)

Figure 1. (a) Antero-posterior and (b) lateral views of the atlanto-axial region, which were non-contributory.

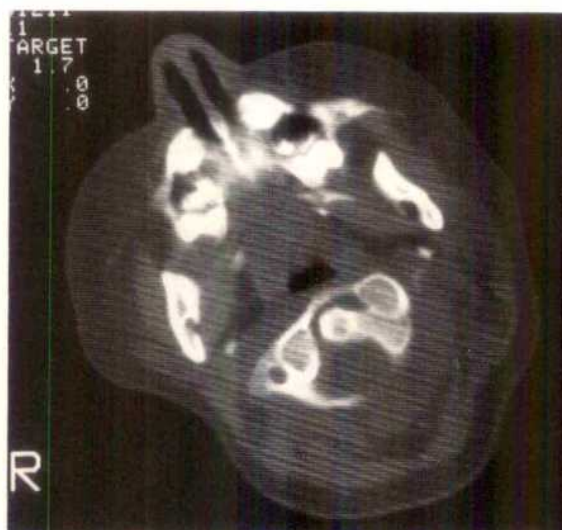
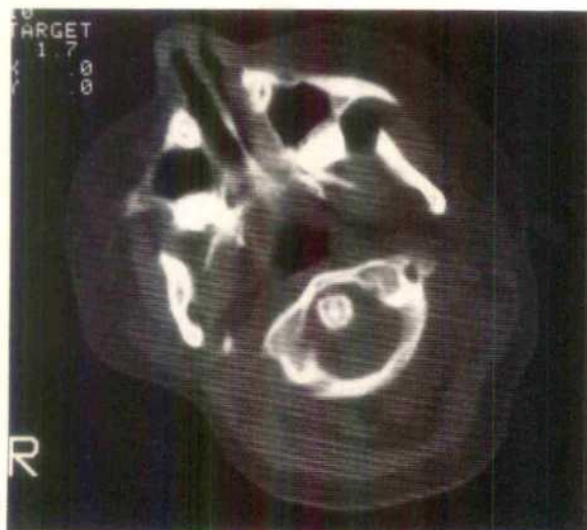


Figure 2. Computed tomographic scans (GE 8800) showing rotation of the atlas on the axis.

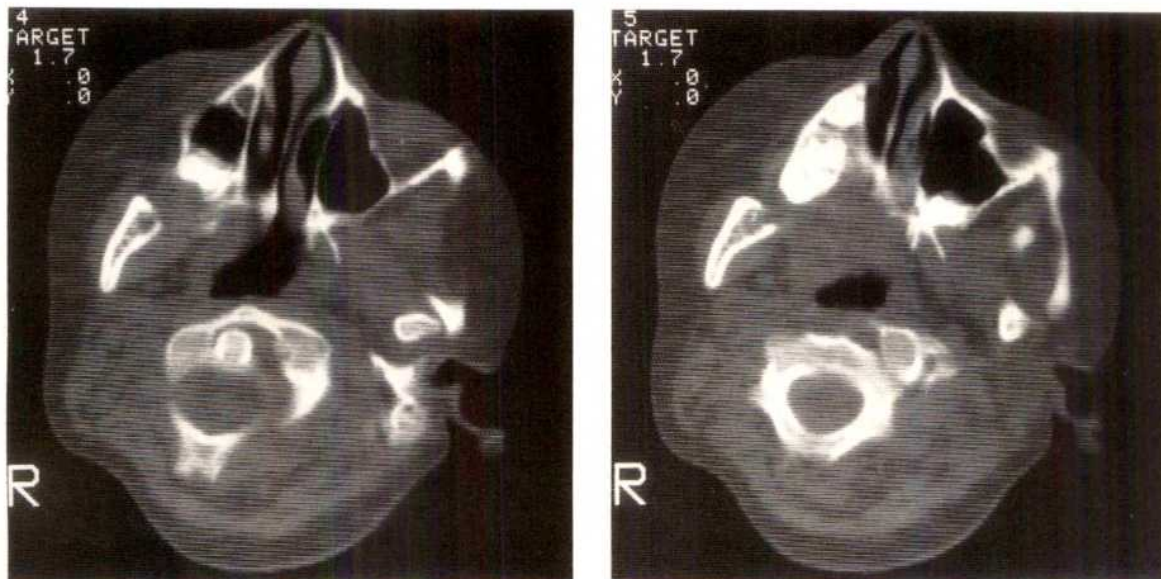


Figure 3. Computed tomographic scans (GE 8800) with the head turned away from the torticollis showing no change in the position of the atlas on the axis.

cephalus. On examination her head was held in the classical "Cock-Robin" position and no movement was possible. There was no neurological deficit. Cervical spine radiographs were not only difficult to obtain but revealed little useful information (Fig. 1). Screening of the neck was attempted but was again difficult and an abnormality of movement could not be excluded.

Under sedation, a CT scan was obtained from the skull base to the top of the vertebral body of C3 using 5 mm contiguous slices with a vertical gantry. This showed rotation (39°) of the atlas on the axis with no widening of the gap between the dens

and the anterior arch of the atlas (Fig. 2). The CT scan was then repeated whilst the patient attempted to turn her head in the opposite direction to the torticollis (Fig. 3). This showed no change in the relationship between the axis and atlas confirming an atlanto-axial rotary fixation.

Skull traction was applied for 4 days with no effect but under a general anaesthetic, just prior to open reduction, the deformity corrected and surgery became unnecessary. After 6 weeks in a "Sumo" collar, plain radiographs and screening of the atlanto-axial region confirmed a full, normal range of movement (Fig. 4).

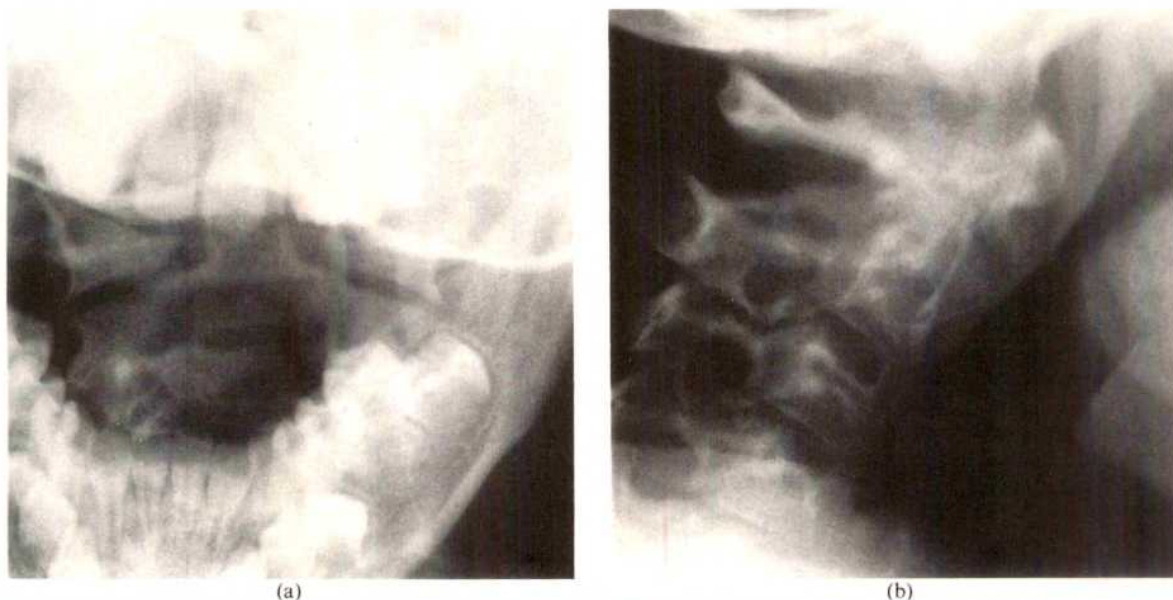


Figure 4. (a) Antero-posterior and (b) lateral views of the atlanto-axial region showing normal alignment of the atlas on the axis.

Discussion

The outstanding feature of atlanto-axial rotary fixation is fixation of the atlas on the axis in a position normally attained during rotation. The plain radiographic features may be confusing because of difficulty in positioning the patient and interpretation of the radiographs. Computed tomography was first used for this condition in 1978 (Fielding & Hawkins, 1978). However, a recent elegant study (Kowalski et al, 1987) emphasized the fact that a single scan cannot distinguish a simple torticollis from atlanto-axial rotary fixation or indeed from a normal volunteer mimicking the "Cock-Robin" posture. The fixation must be confirmed by repeating the scan whilst the patient attempts to correct the deformity. A simple torticollis will demonstrate movement between the atlas and axis.

The aetiology of atlanto-axial rotary fixation remains unclear. It has been suggested that swollen capsular and synovial tissues together with muscle spasm play a part (Fielding & Hawkins, 1977). Certainly, many cases

appear to complicate an upper respiratory infection or mild trauma and the latter may have been responsible in our case.

This entity is rarely considered early enough in the assessment of a torticollis, with the mean delay to diagnosis in the literature being 11.6 months (Fielding & Hawkins, 1977). We suggest that any torticollis that appears resistant should be investigated by a functional CT scan, and early diagnosis as in this case may avoid surgery.

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Case of the month

A rare diversion?

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(Received March 1988)

A 47-year-old man attended for a lymphogram in October 1986. In January 1983 he had been treated for a retroperitoneal teratoma with radiotherapy and chemotherapy. Response was good and he remained tumour-free until clinical examination, at routine follow-up in August 1986, revealed a left testicular mass. When excised, this proved to be a seminoma. Review of histology confirmed this to be a second primary tumour. In addition to computed tomography (CT), he was referred for staging lymphography.

A bipedal lymphogram was performed, giving 12 ml of lipiodol ultrafluid in total. The patient suffered no ill effects and returned 24 h later for standard follow-up radiographs and an intravenous urogram (IVU) (Fig. 1).

What abnormalities are present and what possible causes are there for each? Can these be accounted for by a single diagnosis?



Figure 1. Thirty-minute IVU at 24 h after a bipedal lymphogram.

The radiograph from the lymphogram/IVU series demonstrates diffuse reticular opacification of the liver, absence of lymph node filling above L4, destruction and collapse of the bodies of the second and third lumbar vertebrae and slight displacement of the left kidney laterally.

The possible causes of widespread liver opacities include neoplastic, infective and pharmacologic aetiologies (Darlak et al, 1980). Hepatomas, cholangiocarcinomas and haemangiomas of the liver all calcify rarely. The commonest metastases causing calcification in adult livers are from colloidal carcinoma of the colon and rectal carcinoma, but it may also occur with metastases from almost any source. This type of calcification is described as amorphous, flakey or fine punctate, stippled, granular or of poppy seed appearance, rather than the reticular pattern seen in this patient.

Infective causes of liver calcification include tuberculosis, hydatid disease, coccidiomycosis, amoebiasis, syphilis, histoplasmosis, brucella, and schistosomiasis, and it is usually punctate or nodular in appearance. Thorotrast may be trapped in the reticuloendothelial system causing a reticular pattern of opacification, but the spleen is also involved.

The cause in our patient was embolization of lipiodol to the liver via lymphatico-portal venous anastomoses; the reticular pattern is typical of hepatic oil embolism (Ngan & James, 1978). This is a rare complication of lymphography (0.19–0.7% in different series) occurring in patients with obstruction of upper abdominal lymphatics due to destruction of lymph nodes by tumour (Silverstone et al, 1984), radiotherapy, filariasis (Chavez et al, 1968), surgical block dissection (Donaldson et al, 1984), and retroperitoneal fibrosis with or without inferior vena cava obstruction. The occlusion of lymphatic channels is thought to allow lymphatic-portal venous anastomoses to open and contrast medium to flow to the liver where it is trapped in the finest portal vein branches. This results in either a fine reticular or granular pattern in the liver, which may be difficult to recognize on plain radiographs, and cause confusion on CT and ultrasound imaging (Silverstone et al, 1984). It generally disappears from the liver over some months. As in all cases reported in the literature, there were no unpleasant or dangerous sequelae, or even a rise in liver enzymes. Our patient had originally been given radiotherapy after needle biopsy diagnosed his teratoma in 1983 (Fig. 2). It is likely that the initial extensive tumour and radiotherapy had caused permanent lymphatic destruction sufficient to produce hepatic oil embolism and absence of node filling above the fourth lumbar vertebra.

In summary, hepatic oil embolism following lymphography should be included in the differential



Figure 2. Intravenous urogram from January 1983 showing a left para-aortic mass displacing the left kidney, and destruction of part of L2.

diagnosis of liver opacification. This is particularly relevant in patients undergoing CT as the contrast medium may remain in the liver for months, and increased liver density may be apparent when no increased opacification is visible on plain radiographs.

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Short communication

Clinical evaluation of a digital signal-processing device for real-time speckle suppression in medical ultrasonics

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(Received February 1989 and in revised form March 1989)

Although the field of medical ultrasound imaging has experienced significant advances during the last few years, ultrasound images still suffer from a type of acoustic noise called speckle, which represents a major source of image quality degradation (Kremkau & Taylor, 1986). Speckle is an interference effect caused by the addition by the transducer of echoes scattered by tissue inhomogeneities of size and spacing too fine to be resolved (Morrison et al, 1980; Wells & Halliwell, 1981). The resulting granular pattern depends on both the imaging system and the tissue being imaged in such a complicated way that, although it could be possible to use the statistical properties of speckle for tissue characterization (Wagner et al, 1987), a human observer cannot isolate the true tissue information simply by visual inspection of the image. There are several reasons that make a speckle-free image desirable.

1. Speckle limits the resolution of small structures and reduces the ability of a human observer to detect low-contrast lesions (Smith & Lopez, 1982; Lowe et al, 1988).
2. Since speckle is a machine-dependent artefact, it introduces unnecessary image variability between different scanners (Chivers et al, 1986).
3. The human visual system is very sensitive to random intensity fluctuations (noise). Although no experimental data exist for medical ultrasound, it has been observed in other areas where this phenomenon is also encountered, that speckle reduces the efficiency of a human observer by causing viewer fatigue (Rawson et al, 1976).

The need to produce a smooth image has been acknowledged by the manufacturers of commercial equipment. Simple digital signal-processing techniques such as frame-to-frame and spatial averaging are common features of all modern ultrasonic scanners. However, these techniques cannot be used to suppress speckle fully because they will introduce severe blurring and loss of true tissue information.

Recently, more sophisticated computer image-processing algorithms have demonstrated that it is possible to suppress speckle while preserving the important features of the scan (Bamber & Daft, 1986; Loupas et al, 1987). These algorithms are adaptive in the sense that the amount of smoothing performed at each point of the image is adjusted according to some local properties (e.g. mean, variance) of the grey-scale levels inside a small area surrounding that point. However, their major drawback is that, because of the software implementation, they tend to be unacceptably slow and they are clearly incompatible with the real-time nature of an

ultrasound examination. For example, depending on the complexity of the algorithm and the minicomputer used, the processing time for a single frame can be 10^3 – 10^5 times slower than the 0.1–0.04 s needed for real-time operation.

Methods

In order to apply speckle suppression in routine scanning, a new digital filter has been developed that is capable of real-time operation. The filter has been implemented in hardware using TTL and fast memory integrated circuits. It operates on input data digitized to 6-bit accuracy and it can produce a new output value every 150 ns (maximum digitizing frequency 6.6 MHz). The main features of the filter are: processing at video rates; edge/detail preservation; adjustable smoothing; and cheap and simple construction.

In more detail, the filter can process a frame in less than 0.04 s compared with 5 min needed by a DEC PDP11/23 minicomputer, which implements the same algorithm in software. The speed improvement is due to the use of dedicated hardware components that can perform the necessary computations considerably faster than a microprocessor (addition of two 4-bit numbers in 20 ns instead of 1 ms). Another factor is the pipeline structure and parallelism of the circuit, which performs the equivalent of 50 Fortran statements simultaneously. The adaptive nature of the algorithm results in maximum smoothing of areas that contain only speckle but preservation of edges and other important features of the image. The amount of smoothing is adjustable to accommodate different noise levels with the noise variance of the processed image reduced by 20–60%. The prototype has been built on a single board using cheap and widely available components. However, the use of custom-designed integrated circuits could reduce the size and complexity of the circuit even further. A full description of the filtering algorithm and the technical aspects of its implementation in hardware can be found elsewhere (Loupas, 1988).

In order to evaluate the performance of the hardware filter it was decided to apply it to clinical data and examine the effect of processing on image quality, along similar lines to noise reduction evaluation studies in other diagnostic techniques (Jaffe et al, 1982). The filter was interfaced to a GL Ultrasound Ltd Z/S 3.5 MHz mechanical sector scanner, which was then used during routine abdominal scanning to acquire the evaluation data. Two or three suitable anatomical views from each patient were included in the evaluation. For each view, a set of three scans corresponding to no smoothing, light smoothing and heavy smoothing were recorded on X-ray film. In total, 80 sets from 32 patients were obtained but some of

Table I. Means $\pm$ standard deviations of the evaluation marks given by the radiologists (Observers I, II) and the physicists (Observers III, IV)

Image type	Noise	Contrast	Boundary Definition	Diagnostic Information	Overall Quality
Observer I					
Unprocessed image	2.14 ± 0.61	2.67 ± 0.55	2.26 ± 0.65	2.29 ± 0.65	1.91 ± 0.82
Light smoothing	$\uparrow 2.39 \pm 0.72$	2.67 ± 0.53	2.43 ± 0.70	2.33 ± 0.69	1.97 ± 0.69
Heavy smoothing	$\uparrow 2.56 \pm 0.68$	2.69 ± 0.52	2.44 ± 0.70	2.43 ± 0.70	2.12 ± 0.91
Q^*	0.18	$+\infty$	$+\infty$	$+\infty$	0.50
Observer II					
Unprocessed image	2.75 ± 0.58	3.01 ± 0.40	2.79 ± 0.59	2.99 ± 0.59	1.37 ± 0.54
Light smoothing	$\uparrow 2.90 \pm 0.49$	2.99 ± 0.47	2.88 ± 0.56	2.88 ± 0.66	$\downarrow 1.96 \pm 0.68$
Heavy smoothing	$\uparrow 2.94 \pm 0.45$	3.00 ± 0.42	2.82 ± 0.57	2.90 ± 0.60	$\downarrow 2.66 \pm 0.64$
Q^*	0.14	$+\infty$	$+\infty$	$+\infty$	0.50
Observer III					
Unprocessed image	1.10 ± 0.29	2.29 ± 0.63	1.64 ± 0.58	—	2.92 ± 0.32
Light smoothing	$\uparrow 2.12 \pm 0.33$	2.16 ± 0.60	$\uparrow 2.22 \pm 0.60$	—	$\uparrow 1.79 \pm 0.52$
Heavy smoothing	$\uparrow 2.79 \pm 0.40$	2.23 ± 0.54	$\uparrow 2.27 \pm 0.65$	—	$\uparrow 1.29 \pm 0.48$
Q^*	0.14	$+\infty$	0.22	—	0.50
Observer IV					
Unprocessed image	1.17 ± 0.37	1.79 ± 0.50	2.00 ± 0.53	—	2.83 ± 0.50
Light smoothing	$\uparrow 2.60 \pm 0.49$	$\uparrow 2.58 \pm 0.57$	$\uparrow 2.50 \pm 0.62$	—	$\uparrow 1.53 \pm 0.53$
Heavy smoothing	$\uparrow 2.92 \pm 0.36$	$\uparrow 2.74 \pm 0.55$	$\uparrow 2.36 \pm 0.71$	—	$\uparrow 1.64 \pm 0.65$
Q^*	0.18	0.21	0.28	—	0.50

Noise, contrast, boundary definition and diagnostic information graded from 1 (poor) to 4 (excellent quality). Overall quality graded from 1 (first) to 3 (last in order of preference).

*Minimum statistically significant differences between two means at 1% level ($+\infty$ indicates no statistically significant differences).

them had to be excluded because they did not contain anatomically comparable scans. The remaining sets, 73 from 30 patients, were evaluated by two consultant radiologists and two medical physicists.

Five quality indices were evaluated. The observers were asked to give marks to the scans of each set according to their noise level, contrast, boundary definition and, in the case of the radiologists, diagnostic information. The scans were rated on a 4-point scale for each of the above criteria, with 1 indicating very poor quality and 4 excellent quality. The observers were also asked to rank the scans of each set in order of preference with mark 1 given to the best scan of the set. This last category can be considered as an index of overall quality.

Static instead of live images were included in this evaluation because they offered a more convenient and easier to quantify method of comparison. However, since ultrasound imaging is a highly interactive procedure with diagnostic information extracted not from a single view but from a sequence of scans, it is reasonable to assume that the evaluation did not take into account the real-time capabilities of the hardware filter. During experimentation with this device, users were more impressed with speckle suppression applied to live scans rather than with the smoothed frozen image. This suggests that the real-time performance of the hardware filter, although more difficult to quantify accurately, would be more favourable than the results of this study indicate.

Results

The marks given by the observers were analysed statistically to determine if the observed differences between the means of each image type are real or can simply be attributed to chance.

For the noise, contrast, boundary definition and diagnostic information categories the statistical tests were based on two-way classification analysis of variance and the Studentized Range criterion (Snedecor & Cochran, 1980). The marks for the overall quality category, which are ranks, were analysed using the two-way classification Friedman test and a criterion based on the standard normal percentage points (Daniels, 1978).

The means and standard deviations of the evaluation marks for each observer, image type and quality index are presented in Table I. The results of the statistical analysis can be deduced from the Q values, which have been included in the same table and give the minimum absolute difference two means must have so that the corresponding image types can be considered distinguishable at 1% level of significance. The presence of an up-arrow ($\uparrow$) or a down-arrow ($\downarrow$) before the mean of a processed image indicates that this type of processing offers statistically significant improvement or deterioration compared with the original.

From Table I, it can be seen that noise is the only category that exhibits statistically significant differences in favour of the processed images for all four observers. On the other hand, with the exception of Observer IV, the contrast of the processed images was thought to be almost identical to that of the unprocessed images. As far as boundary definition is concerned, all the observers gave higher marks to the processed images but only the results of the physicists are statistically significant. In the diagnostic information category, the radiologists judged all image types to be equivalent. Finally, in the overall-quality category, one radiologist judged processed and unprocessed images to be equivalent whereas the other

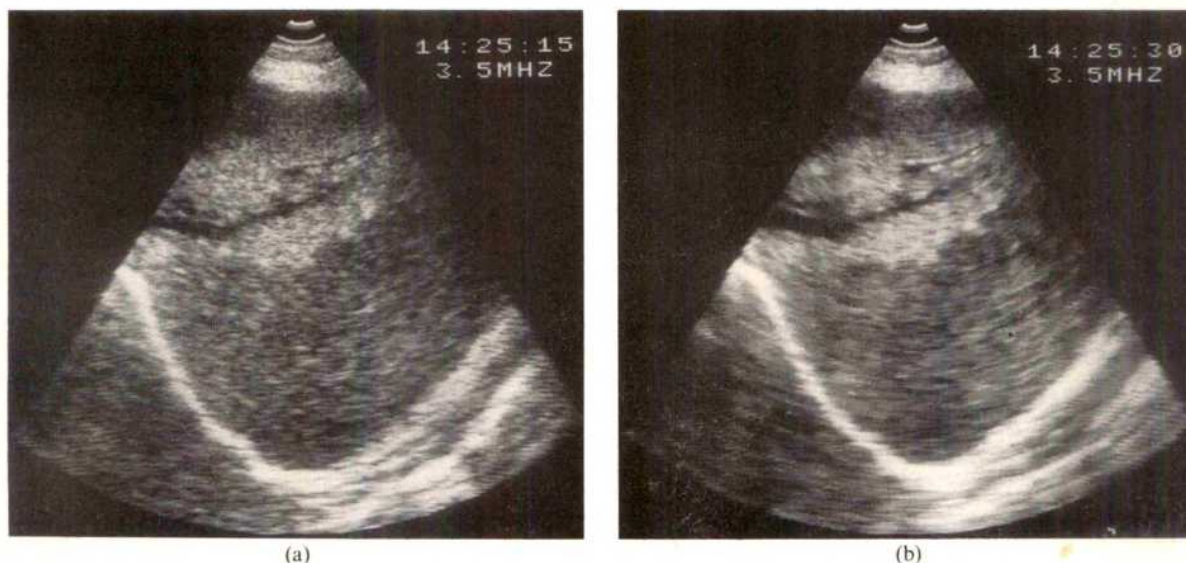


Figure 1. Diffuse liver disease: (a) original and (b) processed (light smoothing) images.

believed that processing produced worse images. On the contrary, both physicists expressed a strong preference in favour of the speckle-suppressed images.

Discussion

From the results of Table I, it is evident that the radiologists and physicists who acted as observers in this study expressed different attitudes towards the processed images and possibly used different criteria to judge the success or failure of processing. This can be attributed mainly to the fact that although interest in acoustic speckle is constantly increasing, it is still confined to the scientific/technical community and, as a

consequence, physicians may not be fully aware of the artefactual nature of speckle. In addition, since speckle suppression is still a research area and has rarely been used in a clinical environment, radiologists have not been exposed to it. As a consequence, they probably feel more confident and are more efficient in interpreting a conventional scan, something for which they have been trained and have accumulated considerable experience, rather than one with suppressed speckle. However, the lack of familiarity should become less of a problem as more speckle-suppression techniques, suitable for application in a clinical environment, are introduced.

An interesting observation, not apparent from the average

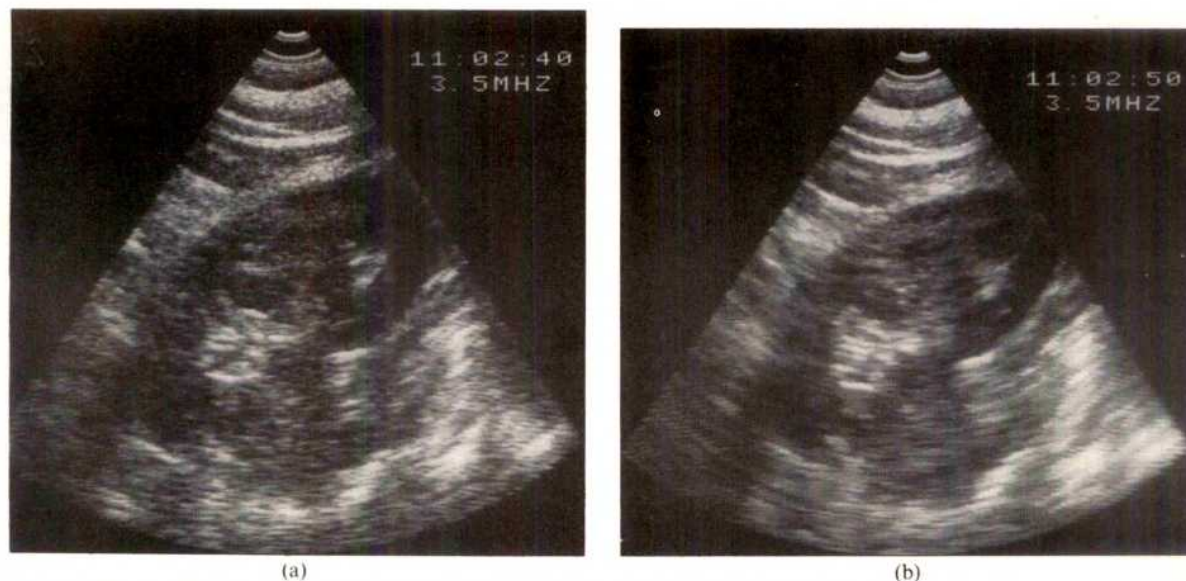


Figure 2. Tumour distal to right kidney: (a) original and (b) processed (light smoothing) images.

ratings of radiologists in Table I, emerged by examining the individual evaluation marks given by the radiologists to the images of each set. In most cases where the processed images of a set were ranked higher than the original in terms of overall quality, they were also judged to have higher diagnostic content and the scans of that set contained pathological findings. In other words, processing was found to be more useful when applied to images containing pathological features. This observation is consistent with our opinion that if real-time speckle-suppression techniques are to be incorporated into ultrasonic scanners, they should not be used to replace the conventional way of presenting a scan but as an alternative form of displaying the echo information in cases of suspected disease in soft tissue. Two examples of speckle suppression that were judged by both radiologists to have higher diagnostic content and better overall quality compared with the originals are presented in Figs 1 and 2.

This clinical evaluation demonstrated that speckle suppression can be performed in real-time without loss of genuine image detail. However, the evaluation did not provide a conclusive answer to the question of how useful speckle suppression is as far as diagnostic information is concerned. From this point of view, the present study can be considered as a first step in the attempt to assess speckle suppression in medical ultrasound imaging. A more powerful hardware filter, which overcomes some of the limitations of the previous design revealed by the clinical evaluation, is currently under construction. With the help of this filter and by carrying out a larger scale clinical trial, it is hoped that it will be possible to determine the clinical usefulness of speckle-suppressed images.

Acknowledgments

The help of Dr S. D. Pye and Dr S. R. Wild who, together with P. L. Allan and W. N. McDicken, participated as observers in the clinical evaluation is gratefully acknowledged. This work was supported in part by the Scottish Home and Health Department.

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Changes in relative biological effectiveness with depth of neutron beams

THE EDITOR—SIR,

The paper by Dr Hornsey and colleagues that appeared in the November issue of the *British Journal of Radiology* (Hornsey et al, 1988) had a pleasantly familiar message. In fact, the principal conclusions drawn were made previously some years ago in papers appearing in the *British Journal of Radiology* describing data obtained on the NASA cyclotron at Cleveland, where neutrons are generated by 43 MeV ($p \rightarrow Be$) (Hall et al, 1982, 1983). The pertinent observations are:

- (1) There is (or may be) a change of relative biological effectiveness (RBE) with depth for high-energy neutron beams.
- (2) The change of RBE with depth can be reduced or eliminated by the addition of a hydrogenous filter.
- (3) The change of RBE is due to a change of beam quality. Hornsey et al (1988) "suggest" this as an explanation, but of course spectral and microdosimetric measurements on several high-energy beams have already established that this is the case.

One further point needs to be made. Hornsey et al (1988) conclude that "It is clear from these studies that with high-energy neutron beams some hardening of the beam as it penetrates tissue will be a normal condition". This statement is much too general in view of the available experience.

The change of RBE with depth is generally *not* seen for high-energy neutron beams generated by deuterons on beryllium, where the neutron spectrum produced has a single peak. This has been confirmed by both biological and microdosimetric measurements and would not be expected, since hardening of the beam with depth by differential filtration of low-energy neutrons is balanced by the production of lower-energy neutrons by scattering.

On the other hand, the change of RBE with depth is not surprising for high-energy neutron beams generated by protons on beryllium, where a wide spectrum of neutrons is produced, including a substantial low-energy component that is filtered out in the first few centimetres of tissue. However, it turns out that the magnitude of the RBE change with depth for neutrons generated by protons on beryllium is very variable from one machine to another. In some cases it is substantial, while in other cases it is barely detectable, even in the same biological test system. It appears to depend critically on the target thickness and design, as well as the design of the collimating system, all factors that have a major influence on the relative size of the low-energy neutron component of the beam.

We would certainly support Dr Hornsey's call for more radiobiological measurements with neutron beams; much is not understood that is of practical concern to the neutron radiotherapist as well as of interest at the level of basic science.

Yours, etc.,

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(Author's reply)

THE EDITOR—SIR,

The comments of Professor Hall are both interesting and pertinent, and indicate that if we are to assess the biological and medical effects of neutrons accurately, we should measure relative biological effectiveness changes with depth not only prior to using a new neutron beam but whenever changes in target construction are made or new beam collimation is introduced.

Yours, etc.,

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(Received April 1989)

Pioneer discovery of rare-earth fluorescence

THE EDITOR—SIR,

Soon after Roentgen's discovery of X rays in 1895, calcium tungstate was found by Thomas Edison and others to be an excellent phosphor for use in diagnostic radiology. More recently, rare-earth phosphors have been used. Buchanan and his colleagues (Wickersheim et al, 1970; Buchanan et al, 1972) have been identified, both in reviews of the subject (Skucas & Gorski, 1980) and in your columns (Rothery, 1989) as the discoverers of rare-earth fluorescence.

In fact, rare-earth fluorescence, under the influence of cathode rays, was identified by Crookes (later Sir William Crookes, of Crookes' tube fame) in 1881, that is to say before the discovery of X rays. Further reports (Urbain, 1905, 1907; Kowalski & Garnier, 1907) discuss the colours of the various emissions of different rare earths, and report measurements of the wavelengths of these emissions.

Whilst I have no wish to denigrate the work of Buchanan and his colleagues in the rediscovery of rare-earth fluorescence and their work to develop modern rare-earth intensifying

screens, the pioneer work of the English and French scientists should not be forgotten.

Yours, etc.,
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Proceedings of The British Institute of Radiology

Radiobiology work in progress

Normal-tissue radiation reactions and their quantification

Abstracts of papers presented at an all-day meeting of the BIR held at the British Institute of Radiology, 36 Portland Place, London W1N 4AT, on Friday, 24 February, 1989

Radiobiology work in progress

Chairman: Dr I. J. Stratford

Radiation-induced delay at the restriction point, by D. L. Dewey

The response of α -irradiated *E. coli* B/r to treatment with penicillin: evidence for the "oxygen-in-the-track" hypothesis, by N. E. Gillies, C. J. Kalman and B. D. Michael

The irradiation of mammalian cells by low-energy protons, by M. Folkard, K. M. Prise, B. Vojnovic, S. Davies and B. D. Michael

Distribution and haemopoietic effects following low-level contamination with plutonium 239 *in utero*, by T. M. Mason, E. R. Humphreys and B. I. Lord

The survival of V79 cells at extremely low radiation doses, by B. Marples, M. C. Joiner, N. J. McNally and J. Soranson

The cellular α/β ratio: is it a constant?, by J. H. Peacock, T. J. McMillan and G. G. Steel

Radiation-induced delay at the restriction point

D. L. Dewey

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There is a well known radiation-induced delay in the G_2 phase of the cell cycle. There is also a less well known and more difficult to measure delay in G_1 . I have developed an automatic pulse-labelling device that allows accurate time measurements of entry into S phase. This equipment has proved to be an ideal method in the study of radiation-induced G_1 delay. The results have shown that for HP2 cells irradiated in G_1 , the magnitude of the delay was not proportional to dose, but was a most unusual relationship for radiobiology; e to the power of the delay time was directly proportional to radiation dose. The formula holds down to very low doses where there was no detectable lethality, thus the mechanism of radiation-induced delay was unlikely to be related to that of cell killing. The magnitude of the delay was independent of the position or age of the cells within G_1 at the time of irradiation, provided the dose was given before a very sharp point in time (about 2 h before S). Cells irradiated after this point have no G_1 delay but they do have a G_2 delay. A change of state is known, for many cell lines, in respect of a number of properties of cells a few hours before S, and is generally called the restriction point. Thus, to obtain a G_1 delay, it was necessary to irradiate before the cells reached the restriction point. The relative biological effectiveness (RBE) for neutrons was very nearly equal to 1 and was thus unrelated to the high values of RBE of the G_2 delay. The oxygen effect on the G_1 delay was a factor of 2.5, which was the same as that for cell kill in this cell line. Using a new technique, to be described, I have found that cells irradiated early in G_1 continue their passage through G_1 after they have been irradiated, until they come to the restriction point, where they wait for the time of the delay. Using another new technique, it can be shown that cells waiting at the restriction point, wait on the early G_1 side of it. Thus cells irradiated in early G_1 , after stimulation to cycle by serum factors, continue their progression through the phase of epidermal growth factor and insulin-like growth-factor modulation, to the point in time where the oncogene *c-ras* is transcribed, where the cells wait for a time proportional to the log of the radiation dose + 1. The effect was independent of the temperature-dependent set-back delay and could be useful as a tool for elucidating the mechanisms involved in the control of the cell cycle.

The response of α -irradiated *E. coli* B/r to treatment with penicillin: evidence for the "oxygen-in-the-track" hypothesis

N. E. Gillies, *C. J. Kalman and †B. D. Michael

*Department of Oncology, University College and Middlesex School of Medicine, London, *Ministry of Defence and †CRC Gray Laboratory, Northwood, Middlesex*

Incubation of X-irradiated *E. coli* B/r with a non-lethal concentration of penicillin causes additional killing provided the cells are exposed under aerobic conditions. We now report on the effect of penicillin on the survival of cells that were irradiated with α particles from ^{238}Pu in the presence or absence of oxygen. The aim was to determine not only the linear energy transfer (LET) dependence of the additional killing by penicillin but to test the hypothesis that a significant amount of oxygen, sufficient to affect radiation sensitivity in an otherwise anoxic environment, is produced in the tracks of a high-LET radiation. The experimental work was complicated by the fact that, unlike the situation in the earlier work, the response of unirradiated cells to penicillin was not entirely predictable so that the effect of a given concentration of penicillin could not be completely controlled. However, despite this difficulty, careful comparison of the response of α -irradiated and unirradiated *E. coli* B/r to treatment with penicillin indicated that survival of the irradiated cells decreased and was independent of the presence of added oxygen at the time of irradiation. This finding is as expected if oxygen were induced in the tracks of the α particles.

The irradiation of mammalian cells by low-energy protons

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Cancer Research Campaign Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex

An experimental system is described for quantifying various radiobiological properties of Chinese hamster V79 cells irradiated by near-monoenergetic protons with energies below 2 MeV. A 4 MeV van de Graaff accelerator is used to provide a beam of defocused protons that emerge through a polymer

window with an energy of 3.5 MeV. A gold foil is used to scatter a small fraction of protons through collimating slits and onto a rotating platter that supports up to 12 cell samples. The platter is arranged so that each sample in turn is swept once through the collimated beam. The speed of the platter determines the dose to each sample. The cells are irradiated as a monolayer on the surface of 13 mm diameter hydrophilic filters. Results are presented for the survival of V79 Chinese hamster cells irradiated by protons at three incident energies (1.90, 1.15 or 0.76 MeV), equivalent to a track-average linear energy transfer (LET) in the cell nucleus of 17, 24 and 33 keV/ μ m. The coefficients, α and β , from linear-quadratic curves fitted to the three sets of data are: $\alpha=0.13 \text{ Gy}^{-1}$, $\beta=0.078 \text{ Gy}^{-2}$ (1.9 MeV); $\alpha=0.33 \text{ Gy}^{-1}$, $\beta=0.066 \text{ Gy}^{-2}$ (1.15 MeV) and $\alpha=1.03 \text{ Gy}^{-1}$, $\beta=0 \text{ Gy}^{-2}$ (0.76 MeV). The relative biological effectiveness (RBE) values at the 10% survival level, relative to 250 kVp X rays are 1.61, 1.91 and 3.36, respectively. If these data are compared with the RBEs for other light ions, then protons appear to have a high level of effectiveness at a significantly lower LET. The data suggest that protons with an LET of about 35–45 keV/ μ m are most effective at killing cells.

Distribution and haemopoietic effects following low-level contamination with plutonium 239 in utero

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This paper describes two time-course experiments where pregnant mice received low levels of plutonium 239 at the start of developmentally significant stages of gestation. Pregnant mice were injected with plutonium 239 (30 kBq/kg) at 13 days gestation (start of major fetal growth) or at 4 days gestation (embryonic implantation). Two per cent of the injected plutonium reached each foeto-placental unit in the first 24 h and was most concentrated in the fetal membranes (greater than maternal skeleton) and placenta. By birth each neonate contained approximately 1% of the maternal activity, with the highest concentration occurring in the liver. Very little activity accumulated over 9 days lactation and as the neonates triple their birth weight in this time the plutonium 239 concentration fell dramatically in all tissues. After contamination at 13 days, the CFU-S concentration in fetal liver, and later in neonatal spleen and bone marrow, was normal. By 4 weeks, post-partum numbers in the marrow, specifically in regions near to the bone, were significantly lower than in the control. By 8 weeks the concentration of CFU-S was severely reduced in peripheral marrow regions although the concentration was normal at the bone surface. As the activity in the neonatal femur was very low and further reduced by 9 days post-partum, these effects were interpreted as residual damage resulting from fetal liver irradiation. Remaining animals in the study were left for longer-term measurements and have shown no ill effect to date. Effects on CFU-S following contamination at 4 days gestation were less marked but significant reductions again developed in peripheral marrow regions. In this case, fetal liver CFU-S were also reduced by 50% although the quantity of plutonium incorporated was lower than in the previous series. This probably reflects damage to a very early embryonic stem cell, although seeding to newly formed spleen and bone marrow prior to birth was not affected.

The survival of V79 cells at extremely low radiation doses

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The response of V79-379A cells to extremely low radiation doses was studied using a clonogenic recognition assay. The life history of a precise number of microscopically located cells was followed from the time of plating until survival assessment using an automated cell recognition system (Palcic & Jaggi; In *Biosensors & Bioelectronic Systems*, ed. by D. L. Wise, CRC Press, Florida). Cell survival was measured after single neutron doses of 0.02–3.0 Gy and single X-ray doses of 0.01 to 10 Gy. Over this dose range, the cell survival after neutrons decreased exponentially with dose. Over the range 0.3 to 4.0 Gy, X-ray response was consistent with an extrapolation from results obtained at higher doses (4–10 Gy) using the linear-quadratic (LQ) model. However, for X-ray doses <0.3 Gy, cells were more sensitive to X irradiation than predicted. At the very lowest doses (0.01–0.05 Gy) X rays were even as effective as neutrons. This increase in X-ray effectiveness is reflected in a decrease in relative biological effectiveness from ~ 3.5 to ~ 1.0 as the X-ray dose decreases from above 0.5 Gy to below 0.05 Gy. It was found that the LQ model could be fitted to the data if the α parameter was allowed to vary with dose. The data indicate a 2.3-fold increase in X-ray effectiveness (*i.e.* α) as the dose was decreased from 0.3 to 0.05 Gy. The decrease in X-ray sensitivity with increasing dose may reflect an increased repair efficiency or maybe induction of repair mechanisms activated by increased levels of DNA damage. Our data suggest that these processes are activated by a dose of ~ 0.18 Gy.

The cellular α/β ratio: is it a constant?

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The α/β ratio has been widely used as a measure of recovery in both normal tissues and tumours. Values of α and β for tumours are usually obtained by computer-aided analysis of dose-survival curves and for human tumour cells have varied from 2.1 to 92 (Fertil & Malaise, 1981). We have used two measures of cellular recovery in order to derive independent measures of α and β in 15 human tumour cell lines of varying sensitivity. Using low-dose-rate irradiation ($\sim 1 \text{ cGy/min}$), recovery was complete during irradiation and cell survival fell exponentially with dose as a function of α only ($\text{SF} = e^{-\alpha D}$). The value of β is related to the recovery capacity of the cells. According to the linear-quadratic (LQ) equation, the split-dose recovery ratio (RR) is highly dose-dependent: $\text{RR} = \exp(2\beta d^2)$. By performing split-dose experiments over a range of doses and plotting $\log(\text{RR})$ against $2d^2$ we get a reliable value for β . Our results show that the α/β ratio calculated from the LQ fit to the acute survival curves varied from 11 to 46. In contrast, when the values were obtained as described above, we came to the startling conclusion that the α/β ratio is constant with a value of 10.3 ± 1.7 .

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Normal-tissue radiation reactions and their quantification

Chairman: Professor C. A. F. Joslin

Blood flow distribution in the stomach and duodenum following mediastinal irradiation in mice, by R. H. K. Gompertz,

R. T. Mathie, A. Michalowski and J. H. Baron

Biomechanical and thickness changes in pig skin after irradiation, by J. W. Hopewell, M. Rezvani, M. Baker and D. Bader

The observation of radiation reactions in patients and their quantification, by S. Dische

Late cosmetic results following brachytherapy for skin cancer, by K. Forbes, D. A. L. Morgan, J. Thornley, R. S. Portington and D. Challoner

The effect of field size on late skin necrosis in man following single-exposure radiotherapy, by S. Chan

Determination of characteristics of normal-tissue radiation effects in patients, by I. Turesson

Radiation damage to the endocrine system in man, by S. M. Shalet

Subjective measurements in the quantitation of normal-tissue damage, by J. R. Yarnold

Blood flow distribution in the stomach and duodenum following mediastinal irradiation in mice

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Acute to chronic duodenal ulceration as an abscopal effect of mediastinal irradiation has been investigated by studying the distribution of blood flow to the stomach and duodenum of mice. Female CFLP mice ($n=45$) weighing 25–35 g were allocated randomly to one of three groups. Group 1 (controls) were not irradiated. Group 2 (irradiated controls) received 18 Gy 250 kV X rays to the upper mediastinum, which does not cause duodenal ulceration. Group 3 ("ulcer" group) received the same dose of radiation to the lower mediastinum, which induces acute to chronic duodenal ulcers in 45% of animals (Michalowski et al, 1983). Mice were studied 7 days later, using $16.5 \mu\text{m}$ microspheres labelled with ^{113}Sn injected into the aortic arch 60 s before sacrifice. Proximal duodenal blood flow was reduced by 40% in the "ulcer" group compared with unirradiated controls (4.5 vs 8.4 ml/g tissue/min; $p<0.05$, Mann Whitney *U*-test). No other significant differences in blood flow were observed, and organ wet weights were unchanged. Within the "ulcer" group there was no difference between mice with ulcer ($n=5$) and those without ($n=10$). Therefore, reduced duodenal blood flow is associated with duodenal ulceration but may not explain individual susceptibility. Since we have shown that vagotomy inhibits gastric acid secretion and prevents ulcer development in this model, we also examined the effect of truncal vagotomy on gastroduodenal blood flow. Mice ($n=32$) were allocated randomly to receive sham operation (simple laparotomy) or bilateral subdiaphragmatic truncal vagotomy (three groups) performed 24 h after either no irradiation (vagotomy controls), upper mediastinal irradiation (controls) or lower mediastinal irradiation ("ulcer" group). Blood flow was measured 7 days later. Despite vagotomy, proximal duodenal blood flow was 35% lower in the "ulcer" group compared with vagotomized unirradiated controls (4.5 vs 8.1 ml/g tissue/min; $p<0.05$, Mann Whitney *U*-test). In addition, gastric blood flow was decreased by 35% from 2.9 to 1.9 ml/g tissue/min in the "ulcer" group post-vagotomy ($p<0.02$) whereas there were no differences among the other groups. Thus vagotomy leads to a reduction in both gastric acid secretion and blood supply, which protects against the consequences of relative duodenal ischaemia.

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MICHALOWSKI, A., UEHARA, S., YIN, W.-B., BURGIN, J. & SILVESTER, J. A., 1983. Alternative types of duodenal ulcer induced in mice by partial X irradiation of the thorax. *Radiation Research*, 95, 78–86.

Biomechanical and thickness changes in pig skin after irradiation

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Changes in the mechanical properties of pig skin have been studied *in vivo*, using a dermal extensometer, after irradiation with a single dose of 18 Gy of X rays. There was no significant change in the stiffness of irradiated skin when compared with unirradiated skin until 9 weeks after irradiation, when the irradiated skin was significantly stiffer. This effect was also found at 12 and 15 weeks after irradiation. When the increase in skin thickness, as a consequence of oedema, was taken into account a significant increase in the unrelaxed elastic modulus of irradiated skin was only seen at 12 and 15 weeks after irradiation. There were no significant changes in force relaxation after extension of the skin over this time period. After the resolution of oedema, which was associated with a significant 15% reduction in the thickness of irradiated skin relative to unirradiated skin, the mechanical properties of irradiated skin were not markedly different from those of unirradiated skin. However, between 30 and 39 weeks after irradiation there was a further wave of dermal thinning resulting in a total reduction in the thickness of irradiated skin relative to unirradiated skin of 26%. This was associated with a rapid rise in the skin stiffness and unrelaxed elastic modulus by ~65 and ~140%, respectively. It was only at these late times after irradiation that the force relaxation of the skin was modified significantly. At 9 and 12 weeks after irradiation, the percentage of fields treated showing a significant impairment in both stiffness and the unrelaxed elastic modulus was dose related, with ED_{50} values of between 12 and 14.5 Gy. This would appear to be a sensitive method for assessing radiation-induced dermal changes since for doses in this range few gross changes are observed.

The observation of radiation reactions in patients and their quantification

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The staging of tumours, the scoring of response and the recording of radiation dose are all standardized by international agreement and this common language is important to research. The situation with regard to the measurement and recording of radiation morbidity is, however, very different. Although there are some internationally used systems such as that devised by the RTOG and EORTC, less than 5% of all published work uses such a system and in most papers the authors devise their own. An internationally acceptable system would obviously be a great advance, but efforts so far have not been successful. A workshop convened by the Medical Research Council in February 1988 met in London and as a result a system based on the elements that make up morbidity has been proposed as a basis for an international system. A "dictionary" of the elements has now been brought together and it is hoped that the scheme will be tried out in centres where there is interest in the accurate recording of radiation morbidity. The careful observation of patients undergoing radiotherapy can yield information of importance to radiobiology. The early and late reactions associated with continuous hyperfractionated accelerated radiotherapy (CHART) given over a 12-day period are showing patterns different from those observed under conventional conditions. Observations in a limited number of patients treated consecutively, and not in a randomized trial, must always be regarded as preliminary. However, the CHART regime would seem to allow the eradication of tumour with a reduction of late damage and this has been shown in the return of hair growth in skin of some patients given a full tumoricidal radiation dose.

Late cosmetic results following brachytherapy for skin cancer

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The low-dose-rate continuous irradiation delivered by brachytherapy techniques would be expected to cause less severe damage to late-reacting tissues than normally-fractionated external-beam irradiation, and so should give better long-term cosmetic results. We have conducted a survey of patients alive and recurrence-free many years after brachytherapy for skin cancer as a preliminary test of this theoretical expectation. We have reviewed the records of patients treated at least 13 years ago for non-melanomatous skin cancer using radioactive moulds. Fifteen patients who were still alive and recurrence-free were traced, examined and photographed. Time since treatment ranged from 13 to 32 years, median 18 years. Gold or radon grains had been the radioactive materials used. The moulds were made of layered, adhesive bandage ("elastoplast mould", "EPM"), with the grains thus applied 0.5 cm above the skin surface, at which level a dose of 55–65 R was specified according to the dosimetry system of Paterson and Parker. Late radiation reactions have been graded by RTOG/EORTC criteria. All late skin reactions were scored 1 or 2 (mean 1.5). No score above 2 was recorded. These results compare

favourably with those of patients treated by external-beam irradiation in this department over the same era. These findings provide clinical validation for the theoretical advantages of continuous low-dose-rate irradiation.

The effect of field size on late skin necrosis in man following single-exposure radiotherapy

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The influence of field size on skin tolerance is of paramount importance in radiotherapy. Studies of acute reactions in man and laboratory animals have shown a strong dependence on the area factor over the range of 1–20 mm diameter field size. However, there are minimal data on the field size effect for late skin necrosis in man following single-exposure radiotherapy (SER). We have analysed retrospectively the incidence of late skin necrosis in the following groups of patients who received SER at this North-West Regional Centre: (1) grid therapy for superior vena caval obstruction, between 1956 and 1985, using a 230 kV machine and an applied dose of 45 Gy ($n=437$) and (2) small superficial skin cancer treated in 1976 using a 100 kV or 45 kV X-ray beam and an applied dose of 18, 20 or 22.5 Gy ($n=1005$; FSD=10 cm). The crude 10-year necrosis rate was 6% for the second group; no necrosis was seen in the first group. The 50% skin necrosis dose calculated using the probit plot are as follows.

Diameter of portal (cm)	TND ₅₀ (cGy)
1	>4500
1.5–2.0	3108 ± 90
2.1–3.0	2936 ± 90
3.1–4.0	2783 ± 371

These data suggest a sharp increase in skin tolerance between field size diameters of 1.5 and 1 cm. If this relationship is also true for other types of normal tissues, spatial fractionation using multiple, small fields of 1 cm diameter may be employed to give an additional dose to the treatment volume without increasing the complication rate.

Determination of characteristics of normal-tissue radiation effects in patients

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Prospective clinical fractionation studies on acute and late reactions in skin have been going on since 1972 at the Radiotherapy Department in Gothenburg. The clinical assay consisted of breast cancer patients irradiated post-operatively to the internal mammary nodes from unilateral or bilateral fields exposed to various dose schedules; 750 fields in 450 patients have been analysed. Schedules with one, two or five fractions per week and two or three fractions per day were evaluated with erythema, desquamation and telangiectasia as end-points. For some schedules, a dose-response relationship was established in a limited dose range, but often there was only one dose group per schedule. These data are suited to analysis by the method of direct analysis of quantal response. This was used in the present study, along with the linear-

quadratic (LQ) model and its generalization, the incomplete repair (IR) model. The repair capacity was similar for erythema and desquamation, with α/β ratios between 7.5 and 11.2 Gy. Unexpectedly, there was no significant time factor during radiotherapy courses up to 6 weeks for erythema and desquamation, but the repair capacity was changed after 4 weeks for both end-points, and α/β increased to between 18.3 and 34.5 Gy. The repair capacity for late telangiectasia differed significantly from that for erythema and desquamation, with α/β values between 2.8 and 4.3 Gy. There was a significant time factor with a characteristic doubling time of about 16 days, when an exponential function for time was used. For the repair kinetics in skin there were insufficient data to obtain precise estimates. A monoexponential fit gave T_1 between 1.1 and 1.3 h for acute effects and 3.5 h for late effects. A 10-year follow-up showed a continuous progression of late telangiectasia. The rate of progression was strongly dose dependent. The steepness of the dose-response curve increases with a higher degree of telangiectasia. In addition, the slope was found to be steeper for a fixed number of fractions compared with using a fixed dose per fraction.

Radiation damage to the endocrine system in man

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Hormones secreted by endocrine glands can be measured in the circulation. A subnormal hormone response to a standard provocative stimulus of hormone release from a specific endocrine gland or a reduction of circulating hormone levels under physiological conditions can therefore be used as a marker of radiation-induced damage to an endocrine axis. In man it has been shown that the hypothalamus is more radiosensitive than the anterior pituitary but both may be damaged by irradiation. Growth hormone is virtually always the first anterior pituitary hormone to be affected, irrespective of whether the radiation damage is in the hypothalamus or anterior pituitary. Gonadotrophin secretion is more often but not always impaired before adrenocorticotrophic hormone secretion. Thyroid stimulating hormone (TSH) secretion is the least vulnerable to irradiation damage. The degree of damage to the hypothalamic-pituitary axis and the speed of onset of pituitary hormone deficiencies are dose dependent. Both the fractionation schedule as well as the total dose of irradiation are important factors influencing the impact of irradiation damage. The thyroid gland may be damaged directly by external irradiation. The vulnerability of the thyroid to such damage is age-dependent in that individuals younger than 20 years old are more susceptible. Radiation-induced thyroid dysfunction may be reversible but is more often permanent. The biochemical signs of thyroid dysfunction reflect the degree of damage to the gland. The least damage is associated with normal basal TSH and thyroxine (T4) levels and an exaggerated TSH response to thyrotropin releasing hormone

(TRH), progressing to an elevated basal TSH level and a normal T4 level followed by frank hypothyroidism (raised TSH, low T4 levels). Radiation-induced damage to the ovary is dependent on the age of the patient, the total irradiation dose and possibly the fractionation schedule. The older the woman then the lower the total radiation dose required to induce ovarian failure. In men, the germinal epithelium of the testis is damaged by low-dose irradiation but Leydig cell steroidogenesis is only impaired by higher doses of testicular irradiation. In contrast to the female, Leydig cell function in pre-pubertal boys is more vulnerable to radiation damage than in adult males.

Subjective measurements in the quantitation of normal-tissue damage

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Treatment tolerance is a clinical concept describing the impact of injury to one or more normal tissues on a patient's ability to function. Under these conditions, subjective measures of structural and functional changes in tissue/organ systems may be superior to some objective measures in terms of validity, reproducibility, dose-response relationship and feasibility. For example, as part of a prospective randomized evaluation of prophylactic cranial irradiation in good-prognosis small-cell lung cancer patients, a watch policy (no radiotherapy) is being compared with two dose levels of fractionated daily treatment in terms of disease control and late effects on the central nervous system. In this context, subjective assessments of intellectual ability and impact on daily life are the clinically relevant (*i.e.* valid) end-points, which are measured using pre-tested scales applied by physicians and patients on an annual basis. The scales are expected to be sensitive to the two dose levels of the study. Patients with common solid tumours treated with curative intent are given radiation doses close to the limits of tolerance. A full range of observed normal-tissue responses is usual, from no structural/functional disturbance to severe change. The steepness of the dose-response relationship ensures that the probability of moderate and severe normal-tissue damage rises steeply as a function of dose. Subjective scales need to embrace the full range of clinical effect but usually need only a small number of categories (none, mild, moderate, severe) to be sensitive to dose-differences of clinical importance. For example, in a fractionation trial comparing 50 Gy in 25 fractions in 5 weeks to 39 Gy and 42.9 Gy in 13 fractions over 5 weeks to the whole breast after excision of early stage breast cancer, subjective measures of breast shrinkage on a four-point scale form the basis of a reproducible evaluation, which is expected to discriminate 10% differences in total dose. In conclusion, well chosen subjective measures should be just as capable as objective measures of defining isoeffect relationships in fractionated radiotherapy.

Nuclear medicine in gastroenterology

Abstracts of papers presented at a joint IPSM/BIR meeting, held at the BIR, 36 Portland Place, London W1N 4AT, on Tuesday, February 14, 1989

Session 1

Chairmen: Dr A. Smith and Dr A. Parkin

Inflammatory bowel disease, by A. M. Peters. Abstract not received

¹¹¹In white blood cell imaging in acute pancreatitis, by C. Hall, J. P. Neoptolemos, A. Calbreath, D. A. Kershaw and L. K. Harding

Failure of ⁹⁹Tc^m-sucralfate imaging to localize inflammatory bowel disease, by S. P. Lake, A. R. Baker, P. Cosgriff and E. M. Watkin

Indium-111-labelled granulocytes as a method of diagnosing reservoir inflammation following restorative proctocolectomy, by W. A. Kmiot, L. K. Harding, W. H. Thomson, S. R. Hessewood, P. R. Morgan and M. R. B. Keighley

Radionuclide imaging in benign oesophageal disease: the Bradford approach, by G. C. Hart, A. J. Mearns and J. A. Cox

¹¹¹In white blood cell imaging in acute pancreatitis

C. Hall, J. P. Neoptolemos, *A. Calbreath, *D. A. Kershaw and *L. K. Harding

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It has been suggested (Anderson et al, 1983) that ¹¹¹In autologous white blood cell (WBC) imaging may be an accurate prognostic factor in predicting the severity of an attack of acute pancreatitis. We have compared ¹¹¹In WBC imaging 24 h after injection with ultrasound and with the modified Glasgow biochemical prognostic criteria (Leese et al, 1988) in 24 patients. ¹¹¹In imaging was performed at a median time of 6 days from diagnosis of pancreatitis (range 1-14 days) and ultrasonography was performed at a median time of 4 days (range 1-15 days). Biochemical prognostic factors were established within 12 h of admission. Of the three actual clinically severe cases, two had abnormal pancreatic uptake of ¹¹¹In-labelled leukocytes, two had abnormal ultrasound scans and one was predicted by prognostic factors. There were 21 clinically mild cases. ¹¹¹In imaging was equivocally positive in one patient and positive in eight others, with a false positive rate of 9/21. Ultrasound was not performed in one patient and did not visualize the pancreas in five. The remaining 15 ultrasound scans were normal. Prognostic criteria predicted all the mild cases. In conclusion, ¹¹¹In imaging may have a useful role in the detection of severe acute pancreatitis, although in this preliminary study we have found a relatively low specificity (57%) compared with previous reports (Anderson et al, 1983).

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Failure of ⁹⁹Tc^m-sucralfate imaging to localize inflammatory bowel disease

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Visualization of the intestine following oral administration of ⁹⁹Tc^m-sucralfate has been advocated for the investigation of

inflammatory bowel disease. To evaluate this technique, we have studied 11 patients (seven men, four women; aged 18-77 years) undergoing surgery for inflammatory bowel disease and compared the scan appearance with laparotomy and pathological findings. ⁹⁹Tc^m-sucralfate (200 MBq) were given orally 30-36 h before surgery. Each patient's abdomen was imaged at 6 and 24 h after oral administration and 10 of 11 resected specimens were imaged immediately post-operatively. Scans were assessed for presence and distribution of disease by an independent radiologist. Laparotomy and histological examination of the resected specimens confirmed the presence of active inflammatory bowel disease in all patients. The scan appearance was abnormal in eight out of 11 (72%) patients, but concordance between the site of abnormality and actual site of disease occurred in only two (18%). Images of the post-operative specimens were negative in 10 out of 11 (91%) patients. We conclude that ⁹⁹Tc^m-sucralfate imaging is not a reliable method of assessing the extent of inflammatory bowel disease.

Indium-111-labelled granulocytes as a method of diagnosing reservoir inflammation following restorative proctocolectomy

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Total colectomy and ileo-anal pouch anastomosis enables the total excision of diseased mucosa in ulcerative colitis and familial polyposis coli, whilst avoiding a permanent abdominal stoma. However, 5-20% of colitic patients have a poor functional result post-operatively with profuse frequency of defaecation, liquid stool and urgency. We have studied eight patients (four males, four females) with a median age of 25 (range 17-41) years at a median time of 18 (7-35) months post-operatively. Gamma camera scans were performed, including a squat view, at 4 and 24 h following injection of indium 111 in granulocytes. Patients also completed a clinical questionnaire regarding pouch function and had routine blood tests. All patients had a normal peripheral blood white cell count, haemoglobin and erythrocyte sedimentation rate. The median frequency of defaecation in the overall group was 6 (range 4-7)

by day and 1 (range 0–4) by night. Two out of the eight patients had positive scans with a further patient having a borderline positive result. There was increased frequency of fluid stool during the day (median 7, range 6–7) as well as at night (median 2, range 2–4) in the three patients with positive scans, despite antidiarrhoeal medication and dietary restrictions. Indium-labelled granulocyte scanning may be useful in detecting inflammation in those with poor results after ileo-anal pouch anastomosis.

Radionuclide imaging in benign oesophageal disease: the Bradford approach

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The value of radionuclide imaging of the oesophagus is increasingly being recognized, although the debate continues. Our approach is based on erect and supine swallows of 10 MBq

$^{99}\text{Tc}^{\text{m}}$ -colloid in 10 ml and a supine swallow of 20 MBq $^{99}\text{Tc}^{\text{m}}$ -sucralfate in 5 ml. Acquisition is typically in 100 frames of 32×32 , at 0.5 s per frame for each swallow. Processing is usually by condensed dynamic images and time-activity curves. The labelled colloid swallow in the erect and supine positions is a valuable screening test for achalasia and normal peristalsis, although reflux studies give a poor return and are not recommended. The labelled sucralfate swallow compared with the colloid swallow with the patient supine shows the "Bradford Afterglow" for the detection of ulceration. Negative sucralfate imaging commonly indicates that there is no value in endoscopy of the gullet. Overall positive and negative predictive values are 92 and 86%, respectively, when compared with endoscopy. Sucralfate imaging thus allows non-invasive sequential follow-up of healing ulceration. Candidiasis and noxious fluid damage can also now be imaged, giving an early estimate of the potential for fibrosis of the pharynx and gullet. This information has not been available from gastrografin and endoscopy because of the difficulty and danger of these procedures. Results from a range of the above studies are presented to demonstrate the value of dynamic oesophageal scintigraphy.

Session 2

Chairmen: Mr P. Cosgriff and Dr P. J. Robinson

^{75}Se -HCAT: its physiological properties and clinical value, by T. C. Northfield

The use of ^{75}Se -HCAT to assess terminal ileal absorptive function after proctocolectomy, by P. J. Holdsworth, D. G. Nasmyth, L. Burkinshaw and D. Johnston

Evaluation of non-linear modelling techniques in the interpretation of radionuclide gastric emptying studies, by D. Hamilton, A. Dunne, A. Chua and N. Keeling

A reproducible technique for the measurement of gastric emptying, by N. Parr, S. Grime, C. Mackie and M. Critchley
Spreading of rectal drug preparations, by J. G. Hardy

^{75}Se -HCAT: its physiological properties and clinical value

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^{75}Se -HCAT allows, for the first time, non-invasive assessment of the enterohepatic circulation of bile acids in health and in disease. It behaves like a natural bile acid with regard to enterohepatic cycling, hepatic handling, active absorption from the terminal ileum, faecal excretion and overall turnover in the enterohepatic circulation. It differs from natural bile acids in that it undergoes negligible deconjugation by colonic bacteria, so that absorption is confined to the active transport site in the terminal ileum. It therefore provides an ideal substance for testing terminal ileal function. The early conventional retention tests do not correct for colonic retention of ^{75}Se -HCAT and are only semiquantitative. Correction for colonic retention and the measurement of daily ileal absorption efficiency improve the sensitivity of ^{75}Se -HCAT tests to match that of ^{14}C -faecal radioactivity following oral administration of ^{14}C -glycocholate, but without the need for a combustion chamber. A further clinical application of ^{75}Se -HCAT may be to provide a sophisticated assessment of hepatic function by means of hepatoscintigraphy, since it is handled more specifically by the liver than is $^{99}\text{Tc}^{\text{m}}$ -HIDA, and its hepatic uptake, hepatic transit time and biliary excretion can all be studied in a quantitative manner. To date, no information is available on hepatic handling of ^{75}Se -HCAT in patients with liver disease.

The use of ^{75}Se -HCAT to assess terminal ileal absorptive function after proctocolectomy

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^{75}Se -HCAT, a synthetic analogue of a naturally occurring bile acid (cholic acid), was used to assess terminal ileal absorptive capacity after proctocolectomy. We studied 47 patients after proctocolectomy (24 with ileo-anal anastomosis (IAA) and 23 with ileostomies) and 12 normal controls. Of the patients with an ileostomy, nine had <10 cm of terminal ileum resected (I) and 14 had >20 cm resected (I+R). Of the 24 patients with IAA, 16 had a standard pelvic ileal reservoir (IAA+RES) and eight had intact terminal ileum without a reservoir (IAA+TI). ^{75}Se -HCAT retention was measured in a whole-body counter using six NaI detectors. A 1 μCi capsule was administered after a 10-min background count and the activity measured after 2 h to give a basal count; the residual activity was measured after 7 days. Patients with I (median retention at 7 days 15% (3–36)) and both groups of patients after ileo-anal anastomosis (medians, IAA+RES 8.8% (0–23.8); IAA+TI 10.2% (2.7–28.9)) had significantly greater retention of ^{75}Se -HCAT at 7 days than patients who had undergone I+R (median 0% (0–3)) ($p < 0.01$). There was no significant difference in ^{75}Se -HCAT retention comparing patients after IAA+RES with those after IAA+TI or patients with I. All patients after proctocolectomy had a significantly lower ^{75}Se -HCAT retention compared with

the normal controls (median 33.5% (15.6–51.8)). Provided that terminal ileum is not resected, patients who have undergone proctocolectomy retain a proportion of the administered dose at 7 days. Although this is less than in normal individuals, colonic transit could account for this difference. In contrast, excision of the terminal ileum markedly reduces Se-HCAT retention and must be avoided if possible.

Evaluation of non-linear modelling techniques in the interpretation of radionuclide gastric emptying studies

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The analysis of activity-time curves obtained from two-phase radionuclide gastric emptying studies is controversial at the present time. Several techniques for condensing the data for clinical interpretation are in use but their consistency is compromised by the variation in the shape of the curves obtained. We have studied several subjects who each received a light breakfast of which the solid component was labelled with $^{99}\text{Tc}^m$ and the liquid component with ^{111}In . Rapid sequential anterior and posterior imaging enabled good resolution activity-time clearance curves to be constructed from the geometric-mean of this data. Several mathematical models were applied to these curves using microcomputer, non-linear, curve-fitting techniques and an assessment of the suitability of the various models for improving the reproducibility and sensitivity of the technique was made.

A reproducible technique for the measurement of gastric emptying

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We have used gamma camera imaging of radiolabelled test meals to investigate physiology, pathophysiology and pharmacology in both canine and human studies (Parr et al, 1987, 1988a, b). A new method has been described to correct for gastric emptying during the ingestion period, providing a more accurate assessment of the initial emptying phase. The development of an image alignment programme has allowed for correction of subject movement, improving the quality of data acquired from dynamic studies. *In vitro* studies of the dispersion of radiopharmaceuticals in an acid environment have also

been carried out (Parr et al, 1986). Choice of radiopharmaceutical agent and test meal, imaging technique, corrections applied during data processing, and reproducibility of results are discussed. A comparison of canine and human gastric emptying is made, together with an appraisal of the animal model.

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Spreading of rectal drug preparations

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Drugs are administered by the rectal route as both topical and systemic treatments. For topical drug delivery the preparation must spread sufficiently to reach its intended site of action. Systemically-acting drugs are administered rectally as an alternative to oral dosing, for example, in patients unable to swallow or as a means of minimizing drug metabolism by the liver. The extent of spreading of rectally administered, radiolabelled dosage forms has been monitored in healthy subjects. Enema solutions of 100 ml generally spread into the descending colon and occasionally throughout the whole colon. Foam enemas, however, tend to be retained within the rectum and sigmoid colon. The dispersion of suppositories is usually confined to the rectum. Since the venous drainage from the upper rectum is to the portal circulation, the proportion of absorbed drug bypassing the liver will vary according to the degree of spreading. By the appropriate choice of formulation, rectally administered drugs can be targeted to specific regions of the distal colon.

Session 3

Chairmen: Dr M. Buxton-Thomas and Dr A. B. Mostafa

Paediatric liver transplantation: $^{99}\text{Tc}^{\text{m}}$ -IODIDA versus T-tube cholangiogram, by C. P. J. Charlton, L. K. Harding, A. J. Baker, Z. Droc, S. Chapman, M. J. Tarlow, J. Buckels and P. McMaster

Quantifying gallbladder kinetics, by N. R. Williams, Z. Y. Al-Haider, N. J. Tulley, A. B. Mostafa and L. K. Harding

Are pre-duodenal mechanisms important in initiating gallbladder emptying in man?, by S. Ellenbogen, S. A. Jenkins, J. S. Grime, C. R. Mackie and J. N. Baxter

Measurement of duodenogastric reflux in the rat, by M. C. J. Barker, R. H. Diamant and D. Johnston

Paediatric liver transplantation: $^{99}\text{Tc}^{\text{m}}$ -IODIDA versus T-tube cholangiogram

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Prolongation of recurrence of jaundice after orthotopic liver transplantation may be caused by biliary obstruction, rejection, infection or vascular problems. The exclusion of obstruction directs further investigation. Traditionally, a silastic T-tube is introduced across the anastomosis at operation, with one limb in the donor system and the other in the recipient Roux-en-Y jejunal loop. This provides access for cholangiogram imaging of the biliary system. The alternative imaging method with the radiopharmaceutical $^{99}\text{Tc}^{\text{m}}$ -IODIDA does not require presence of a T-tube. We have reviewed the value of these investigations in a series of 14 paediatric liver transplants. Excretion of IODIDA demonstrated patency of the complete biliary system. However, cholangiograms did not adequately indicate patency in the donor system as the contrast flowed freely through the other limb of the T-tube into the Roux-en-Y loop. Furthermore, cholangiography must be covered with antibiotics because of the risk of septicaemia. Excretion of $^{99}\text{Tc}^{\text{m}}$ -IODIDA demonstrates patency of the biliary system: T-tubes are no longer essential in paediatric liver transplants.

Quantifying gallbladder kinetics

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We wished to analyse retrospectively gallbladder and bile duct kinetics in a group of patients who had undergone studies using $^{99}\text{Tc}^{\text{m}}$ -HIDA. The gallbladder in these dynamic studies forms a small image, which varies in size due to filling and contraction. We have examined the influence of the volume and depth on the detection of counts per unit activity (ct/MBq) within the gallbladder region and the quantity and distribution of scattered counts detected outside the region. Data were obtained from a phantom comprising a gallbladder pouch attached to the undersurface of a liver cast, which was submerged in a water bath. The ct/MBq changed with depth and volume and the variation with volume was more pronounced at increasing depth. At 6.0 cm the ct/MBq varied by 14% with volumes ranging from 10 to 60 ml. Ejection fraction calculations were found to be sensitive to change in depth associated with contraction of the gallbladder but not variations with volume. Bile duct activity was quantified in two groups of patients. One group consisted of patients with a functioning gallbladder and the other with a non-filling or absent gallbladder. Taking gallbladder scattering into account, the mean percentage of

injected HIDA in the bile ducts of those with a functioning gallbladder was 6% and 19% with a non-functioning gallbladder ($t=3.6$, $p<0.01$). If scatter was not considered, the corresponding figures were not significantly different.

Are pre-duodenal mechanisms important in initiating gallbladder emptying in man?

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It has recently been reported that gallbladder emptying (GBE) commences in most subjects long before nutrients enter the duodenum (Baxter et al, 1985). These investigators concluded that pre-duodenal mechanisms were responsible for the early GBE following food injection. To investigate whether cephalic and gastric phases of GBE are present in normal subjects, the effect of sham feeding (chew and spit) ($n=30$) and gastric distension (intragastric balloon tube; $n=9$) were studied and compared with normal subjects who ingested a standard meal ($n=14$). A control group given no intestinal stimuli was studied to determine the frequency of spontaneous GBE during fasting ($n=18$). $^{99}\text{Tc}^{\text{m}}$ -EHIDA cholescintigraphy was used as the biliary tracer. The frequency of GBE during fasting was calculated as 0.0045 min^{-1} . Thus in any 20-min period, GBE occurs spontaneously in only one in 10 subjects. Significant GBE occurred in 16 out of 30 subjects following sham feeding ($p<0.001$ c.f. control, Poisson test), in six out of nine subjects following gastric distension ($p<0.001$ c.f. control, Poisson test) and in 14 out of 14 subjects following meal ingestion ($p<0.001$ c.f. control, Poisson test). The rate of GBE was significantly greater following gastric distension and meal ingestion compared with other groups ($p<0.05$, ANOVA). However, GBE rate sham feeding was not significantly greater compared with spontaneous GBE ($p<0.05$, ANOVA). There was no significant difference between groups for time to onset of GBE. These results suggest that both cephalic and gastric stimuli can evoke GBE in man. Contrary to previous belief, pre-duodenal mechanisms appear to play an important role in initiating GBE in most subjects.

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Measurement of duodenogastric reflux in the rat

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Excessive duodenogastric reflux (DGR) has consistently been implicated in the pathogenesis of gastric cancer after operation

for peptic ulcer. In animal studies, it has often been assumed, without direct proof, that DGR was excessive after truncal vagotomy and drainage and partial gastrectomy. Changes in gastric mucosal morphology have been assumed to be due to such putative reflux. However, we know from tests in man that the amount of DGR varies widely within any group of patients after gastric surgery. We have developed a simple method of measuring DGR in rats using $^{99}\text{Tc}^{\text{m}}$ -EHIDA. In preliminary experiments, serial collections of bile confirmed that $^{99}\text{Tc}^{\text{m}}$ -EHIDA is rapidly excreted in the bile of rats after intravenous injection. Further experiments in which the gastrointestinal tract was removed "en bloc" after intravenous injection of $^{99}\text{Tc}^{\text{m}}$ -EHIDA showed how $^{99}\text{Tc}^{\text{m}}$ -EHIDA was distributed along the gastrointestinal tract at various time intervals. We defined a

gastroenteric index (GEI) as the ratio of stomach activity to total intestinal activity; GEI is thus a quantitative measure of bile reflux into the stomach. Using this technique, we measured the GEI in groups of rats (10 in each group) after laparotomy (control), truncal vagotomy and pyloroplasty, truncal vagotomy and gastrojejunostomy and highly selective vagotomy (HSV). The GEI after truncal vagotomy and drainage was significantly greater than GEI after both laparotomy and HSV ($p=0.01$, Mann-Whitney U-test). However, within the truncal vagotomy and drainage groups, GEI varied widely, which is in accord with previous findings in man. The technique described may allow more accurate correlation to be made between measured DGR in animals and the resulting changes in gastric mucosa.

Book reviews

Eurem 88. Volume 1: Tutorials, Instrumentation and Techniques. Volume 2: Physics and Materials. Volume 3: Biology. Ed. by H. G. Dickinson and P. J. Goodhew, pp. xviii + 302, xxx + 582, xxxii + 616, 1988 (Institute of Physics, Bristol), Vol. 1 £32.00, Vol. 2 £60.00, Vol. 3 £62.50, 3 vol. set £123.00.

ISBN 0-89498-184-5 (Vol. 1)
0-85498-185-3 (Vol. 2)
0-95498-186-1 (Vol. 3)
0-85498-187-X (3 vol. set)

These three volumes assemble tutorials, papers and abstracts of posters and oral contributions from the 9th European Congress on Electron Microscopy held in York in September 1988, a total of over 600 selected papers. As the editors say, "the submitted papers reflect the diverse range of applications of electron microscopy in the late 1980s and also the number of complementary techniques which have developed alongside the established SEM and TEM approaches".

Volume 1 contains all the tutorial topics, which cover a diverse range of subjects. I enjoyed this collection of papers, particularly the overview by J. Roth of technical aspects of the colloidal gold marker system, a useful introduction for anyone stepping into this rapidly expanding area of research. Another subject covered is biological cryofixation, an interesting paper, with one of the longest reference lists of any in the three volumes. Other topics covered include Monte Carlo simulation, on-line image analysis and three-dimensional unbiased measurements. There follow six other chapters on instrumentation, commercial developments, image formation and processing, scanning electron techniques, surface analytical techniques and scanning tunnelling microscopy.

Volume 2 contains 15 chapters concentrating on physics and materials. This includes chapters on diffraction, semi-conductors and thin layers, analytical electron microscopy (EM), superconductors and magnetic materials, high-resolution transmission electron microscopy (TEM), metals and ceramics. An interesting and well set out contribution is the opening paper in the chapter on diffraction. This gives a brief review of microdiffraction, giving methods of recording microdiffraction patterns and progress in their interpretation.

Volume 3 contains 24 chapters, concentrating on the applications of electron microscopy to biology. These include chapters on pathology, medicine, invertebrates, plants, analytical EM, image processing, macromolecules, membranes and biotechnology. High-resolution work is still popular, and two examples are the excellent set of micrographs showing the internal structure of the influenza virus and the high-resolution shadowing and imaging of RecA-DNA complexes using both TEM and the relatively new scanning tunnelling microscope.

Image reproduction is good in all three volumes, and a nice feature is the provision of indices for both subjects and authors. My only real criticism is that the varying typeface throughout the volumes is slightly disconcerting when browsing from chapter to chapter, and it is unfortunate that a particular typeface was not stipulated.

There is something for everyone within the three volumes, though not everyone will be able to afford the £123 for the complete set. However, libraries should find it worth purchasing.

K. M. S. TOWNSEND

Hodgkin's Disease and Non-Hodgkin's Lymphomas in Adults and Children. Ed. by Lillian M. Fuller, Frederick B. Hagemeister, Margaret P. Sullivan and William S. Velasquez, pp. xiv + 498, 1988 (Raven Press, New York), \$99.00. ISBN 0-89004-795-2

This very attractively produced, well illustrated book sets out to be a didactic comprehensive text "that is organised to provide practical assistance in the day to day treatment of the individual patient". It is unusual in dealing with both Hodgkin's disease and non-Hodgkin lymphomas and with the management of both adults and children. This unifying approach is both logical and welcome although perhaps it leads in some places to a certain sketchiness and avoidance of controversy. This lack of adequate discussion of controversial areas is probably influenced by the choice of authors: of the 25 contributors, 21 are from the M. D. Anderson Hospital, the remaining four all being contributors to one chapter only, that on mycosis fungoides.

The book is divided into three sections. The first deals with lymphoma diagnosis, biology and staging, the second mostly with the management of Hodgkin's disease and the third with non-Hodgkin lymphomas. This plan works fairly well although there is inevitable repetition, particularly over matters relating to staging and pre-treatment work-up.

In the first section, the chapters on history, immunobiology and immunological characterization of lymphomas are excellent and right up to date. Less so are those on imaging procedures. Here, although the pros and cons of lymphography and computed tomographic (CT) scanning are well covered there is little about the interesting new area of high dose ^{67}Ga scanning and nothing at all about magnetic resonance imaging. Staging laparotomy is presented as an essential in early-stage Hodgkin's disease in adults despite the fact that it has been shown not to influence survival and has largely been abandoned in many other centres. It is even advocated in children, a practice which many would now regard as dangerous and dated in view of the very good results that can be obtained with extremely conservative management.

In general the section on the management of Hodgkin's disease represents orthodox North American practice. Here I would have liked to see a wider perspective.

The chapters on the management of low-grade and high-grade non-Hodgkin lymphomas in adults and children are comprehensive and stimulating although a rather aggressive approach is adopted toward low-grade tumours. These are followed by an outstanding chapter on the complex group of diseases now known as peripheral T-cell lymphomas.

The book concludes with good coverage of mycosis fungoides, the management of relapse in non-Hodgkin lymphomas, bone marrow transplantation and lymphomas in patients with immunodeficiency states.

The choice of edited multi-author publications on lymphomas is considerable at present and this book is an interesting addition to them. Its strongest point is its coverage of all lymphomas in all age groups. Its weakness is its rather parochial single-centre bias, particularly with respect to Hodgkin's disease.

I would recommend it for its outstanding sections on lymphoma pathology and its stimulating approach to non-

Hodgkin lymphomas, but it is a book for the departmental library rather than the personal collection.

T. J. McELWAIN

Time, Dose and Fractionation in the Radiation Therapy of Cancer. A Frontier Revisited. Ed. by J. M. Vaeth and J. Meyer, pp. x + 193, 1988 (Karger, Basel), £81.40; SFr 179; DM 214; US \$119.50.

ISBN 3-8055-4654-8

The sections in this book are derived from papers given at the 22nd San Francisco Cancer Symposium in 1987. Fractionation was also the theme of the 1967 symposium, and the editors point out that in the intervening decades, despite progress in heavy particle irradiation, brachytherapy, hyperthermia, sensitizers and monoclonal antibodies, optimal administration of ionizing radiation remains uncertain. The papers examine this uncertainty in great detail and nearly all the main workers currently involved in the investigation of fractionation are represented here.

It is a very thorough description of the state of the art, directed at the clinician rather than the radiobiologist, who may feel that the experimental field could have been accorded more space. After introductory chapters by Withers, Cox, Hall and Kallman, the main emphasis of the contributions is on clinical studies. Subjects include twice-daily fractionation, three fractions per day, accelerated fractionation, and the significance of fractionation at different sites and for different tumour types. Unfortunately, whilst many clinical studies of altered fractionation have been done, understandably there have been relatively few closely controlled randomized clinical trials of fractionation, and because of the relatively small size of most of these, any conclusions drawn from those that have been done are at best tentative. But these studies will act as a valuable guide to the direction that future trials should take.

Little of the material is entirely fresh to the informed reader, and most of the authors have written on these subjects at length on previous occasions, but it is a useful volume for those interested in fractionation to have in their libraries as a convenient reference. This is not to indicate that it is not a readable volume; the presentations are agreeably short and well presented, with one or two exceptions. It is elegantly produced and well printed, but its price approaches that of the major textbooks in oncology, which may deter the general reader from buying it.

K. DURANT

Haematopoiesis: Long Term Effects of Chemotherapy and Radiation. Ed. by N. G. Testa and R. P. Gale, pp. xviii + 413, 1988 (Marcel Dekker, New York), \$115 (US), \$138 (other).

ISBN 0-8247-7938-X

This multi-author book is an authoritative review of the long-term effects of chemotherapy and radiation on bone marrow function. The editors must be commended on their choice of authors who have not only made contributions to the field but are also able to write clearly and concisely. The bibliographies at the end of each chapter are in general good and will be of considerable help to the reader wishing to pursue an issue further.

The book begins with an excellent review of the structure and regulation of the haemopoietic system and then proceeds to document the damage that occurs to the haemopoietic stem cells and the marrow microenvironment in both experimental animals and in man. There is inevitably some overlap and

repetition in the different chapters but this does allow each chapter to be read as a separate entity. The book poses more questions than it provides answers but this is a reflection of the "state of the art" rather than a criticism of the authors' accounts. This is particularly evident in the sections dealing with marrow damage in man where it is readily apparent that the investigational tools available are still inadequate and that the results obtained are open to numerous explanations.

This book will be of particular value to experimentalists with an interest in haemopoiesis and bone marrow transplantation. Clinicians involved in the management of cancer will also be rewarded by dipping into this book but will probably not want to have their own personal copy at a price of \$115 (US). It can be argued that concern over long-term damage to the marrow is a luxury to the oncologist that is only affordable in situations where cure is expected and these situations are still few in number. The potential problems of adjuvant chemotherapy are particularly worrying but lack of information prevents this receiving more than brief attention. Overall, the editors and authors are to be congratulated on compiling a learned work.

DAVID LINCH

Effective Use of Computers in Nuclear Medicine. Practical Clinical Applications in the Imaging Laboratory. Ed. by Michael J. Gelfand and Stephen R. Thomas, pp. xvi + 604, 1988 (McGraw-Hill, New York), £65.00.

ISBN 0-07-023093-5

This book covers 590 pages of text and is divided into 26 chapters covering every situation in which computing is applied to nuclear medicine. The volume, competently edited by Michael Gelfand and Stephen Thomas, employs about 38 additional authors, but with Gelfand taking the brunt of the writing.

Subject matter covers basic principles (computer acquisition and processing, quantitation of *in vivo* radioactivity and single photon emission computed tomography (SPECT) in three chapters); nuclear cardiology (nine chapters); cerebral SPECT (two chapters); renal nuclear medicine (three chapters); radionuclide studies in gastroenterology (three chapters); orthopaedic radiology, (three chapters—one shared with gallium studies) and three miscellaneous chapters dealing with skin perfusion, parathyroid scintigraphy and lung imaging.

The text assumes a fair degree of basic nuclear medicine knowledge on the part of the average reader, with the result that, from time to time, the going can be a little hard on the registrar in training, especially if lacking in mathematical ability and unfamiliar with jargon—this in spite of the authors' protestations to the contrary. On the other hand, especially in the more clinical sections, the treatment is simplistic. Nevertheless, on the whole, the book finds the right balance and covers most of the topics comprehensively and well. Certainly, for the practising physician, it is useful to have all the techniques and formulae set out in one place for easy reference.

This is particularly the case for the less commonly used procedures and it was, for example, gratifying to find Silberstein's little account of the evaluation of skin perfusion. This is an example of a study that, whilst not routine in many hospitals, is nevertheless still called for occasionally by clinicians and research workers and the easy reference can be very useful. The same goes for Heyman's excellent account of gastroenterological applications.

Although the bulk of the book is not unexpectedly devoted to cardiac studies, I personally found the renal sections to be the most clearly written and practically useful. One of the

disadvantages of multi-authorship is the diversity of writing styles which it seems no editor can entirely eliminate or integrate. It also leads to individual authors occasionally being tempted to ride their favourite research bandwagons at the expense of the more useful routine applications. The advantage of the diversity, on the other hand, is the wide range of opinions and the varied expertise that that can be elicited. This book probably veers towards the latter, more favourable extreme.

The illustrations, although plentiful (266 black-and-white, 31 colour) are not always state-of-the-art and possibly reflect a long gestation period for the book. Unfortunately, many of the scintigrams, which were obviously originally in colour, had to be represented in black-and-white, with consequent lack of resolution in the reproduction. It is difficult to get around this problem. The line drawings, on the other hand, are clear.

The book has a pleasant layout and font, but tends to look a little "crowded" because of a narrow right-hand margin. The left-hand margin is, however, wide and suitable for annotation. There are ample and appropriate references following each chapter which are about as up to date as is possible in a book.

This book is certainly to be recommended as a bench book in all departments of nuclear medicine, and while it should be in all medical school and hospital libraries with an interest in nuclear medicine, I am less certain how useful it would be to the individual physician or radiologist. Certainly it is felt that the trainee should start with something simpler and get a feel for the studies before delving into the book. However, at £65, it is not expensive for all the information it contains and it does at least fulfil the aims set out in its preface.

B. J. SHEPSTONE

Ultrasound of the Abdomen. Exercises in Radiological Diagnosis. By Catherine Roy, pp. vii + 203, 1988 (Springer-Verlag, Berlin), DM 35.

ISBN 3-540-16546-0 (Berlin)

0-387-16546-0 (New York)

This book is the seventh in the series and is intended to illustrate a wide range of conditions in which abdominal ultrasonography is useful in diagnosis. It is written in the form of a series of exercises with ultrasound illustrations on the left-hand page and explanatory text and schematic drawings on the right. A total of 114 separate exercises are present and proceed logically through the biliary tree and liver, pancreas, adrenal glands, kidneys, spleen and miscellaneous structures. The exercises themselves become more difficult as we proceed through each section of the book.

The text is divided into sections of clinical information, description of the ultrasound, diagnosis and comments. The comments section, which is usually the longest, includes technique and the appropriateness (or otherwise) of ultrasound, other relevant investigations and pathological considerations.

The layout is useful when using the book as a study guide, the drawings being helpful in interpretation of the images (although the French initials for organs are slightly irksome). Apart from the initials, the drawings are well labelled although it would be more helpful if they were always adjacent to the relevant text. The reproduction of the ultrasound images is of good quality, sometimes difficult to achieve in ultrasound, which depends so much on real-time imaging. All images are presented in the white-on-black format.

Normal scans of each organ are included at the beginning of the sections on the biliary tree, liver and pancreas but not those on the kidney, adrenal or spleen. These and the accompanying

comments would be helpful to beginners in ultrasound imaging as well as to those at whom the book is aimed.

Most of the important common conditions pertaining to the organs of the abdomen are covered, with the exception of trauma, which has been deliberately excluded. This is a pity as the general principles of abnormality are not markedly different from organ to organ. I also felt that it would have been useful to include a section on the urinary bladder with the kidneys, as ultrasound of the entire urinary tract (for example for haematuria) is a common request. Both bladder and prostatic tumours may be imaged per abdomen and in addition are an important cause of upper urinary tract abnormality, which should be searched for as part of the investigation. It is important to stress that no part of the abdomen should be scanned in isolation, and the chance to emphasize this has been lost here.

There is rather too much of the "this is easy" type of comment in the diagnosis section as often ultrasound appearances are not easy to interpret, particularly in the absence of adequate clinical information. The majority of the information in the comments section was useful and included more general considerations to be taken into account once a diagnosis has been reached, such as associated conditions and predisposing factors.

There are a few problems of translation. On one occasion this has led to a mistake in the diagnosis section of the text. Usually, however, the terms, although not commonly used in English, are understandable (such as sub-febrile for hypothermia). These irritating mistakes should, however, have been prevented by using an appropriate proof reader.

In general, however, I felt that the book would be useful both as an inexpensive study guide and as a quick reference book to help junior radiologists and radiographers learning the technique as it covers most of the relevant pathology except trauma and pelvic abnormalities.

A. J. JONES

Magnetic Resonance Imaging in Diseases of the Nervous System: An Introduction. By Ivan Moseley, pp. vi + 234, 1988 (Blackwell Scientific Publications, Oxford), £39.50.

ISBN 0-632-02052-0

Worldwide sales of magnetic resonance imaging (MRI) units are now probably in excess of 1000. With the entry of the major Japanese imaging conglomerates into the field, the future cost of buying and maintaining a system should fall, especially with the introduction of low-field units employing permanent magnets. The end result will be the greater accessibility of MR scanners to non-specialist centres, following the pattern of computed tomographic scanning. It is therefore appropriate that a textbook should have now been produced that will help make MRI of the central nervous system more amenable to the generalist whilst providing a useful primer for trainees within the spectrum of interest of the neurosciences. The feature of this book that is most striking is the pragmatic and clinically orientated approach taken to MRI, setting the examination in the context of problem orientated investigation. To this end the author has succeeded in his aims. There is a refreshing candour in the approach to scanning that is often lacking in some of the literature and textbooks now prevalent.

As in any text dealing with the subject, a preliminary chapter is devoted to the physics and practicalities of MR scanning. What is provided is a rather simplified overview with, necessarily, considerable generalizations in terms of image generation and sequence choice. A reasonably comprehensive list of references is, however, provided and there is a useful glossary of the more commonly encountered terminology.

The subsequent chapters are laid out in problem orientated sections rather than a catalogue of pathological entities, making easier reading. In general, the chapters are well laid out and the text concise and relevant. However, there are several errors in the layout of some of the figures. Inevitably there are a number of broad generalizations in dealing with some of the more rarefied topics, which are, however, not the brief of such a book. The image quality is variable and in certain cases, where the illustrations are far from optimal, the use of more annotations would have been helpful. Not surprisingly newer techniques have evolved since the time of writing, and with the introduction of paramagnetic contrast agents like gadolinium-DTPA there will be further modifications to scanning techniques. This does not detract, however, from the aims of this book, which I would commend to both the departmental library of any training institute with an interest in this sphere and, being sensibly priced, to those trainees venturing into the field of MRI and the neurosciences.

T. JASPAN

Atlas d'IRM de l'Encéphale et de la Moelle. By E. A. Cabanis, D. Doyon, Ph. Halimi, M. T. Iba-Zizen, R. Sigal and J. Tamraz, pp. x + 148, 1988 (Masson, Paris), 295 F. ISBN 2-225-81294-2

The French neuroradiologists have a long and praiseworthy tradition for establishing a sound understanding of the anatomy of the central nervous system as the basis for correct and meaningful interpretation of all radiological examinations. This atlas is specifically aimed at the anatomy displayed by magnetic resonance imaging (MRI), which has now become the pre-eminent neuroradiological tool. The wealth of information, both anatomical and pathological, provided by this technique further underlines the necessity of a comprehensive yet easily accessible and comprehensible atlas.

The preliminary chapter is devoted to a brief and simplistic introduction to the physical principles of MRI scanning. Although of undeniable importance, the fact that this potentially difficult and complicated subject is dealt with so briefly and in French only renders this chapter somewhat superfluous to the average anglophonic reader. A brief synopsis of the scanning technique employed is given in the subsequent chapter; however, again a good understanding of the French language is needed for fuller appreciation.

The cranium and spinal column are displayed in all three orthogonal planes, each section being displayed by a cadaveric anatomical slice with a corresponding T_1 -weighted MR image. The quality of the images, both anatomical and MR, is generally good; however, accepting the difficulties of correlating the two, it is a little disappointing that the MR images are not also annotated. Fortunately, most of the anatomical terminology is given a satisfactory English translation (with a few notable exceptions) making the atlas readily usable. Less satisfactory is the rather irritating lack of text given in the legends of several sections as enumerated in the figure (e.g. Fig. 6A) as well as the inconsistency of labelling anatomical structures occurring in contiguous slices. There are also too many errors in the labelling of certain structures in several figures, and in other figures the labelling is completely omitted from the image. Regrettably, although the text for the cadaveric section is adequately translated, the same does not apply for the MR image text, even though it is rather brief and at times lacks pertinency.

The images in the spine are generally of a reasonable quality, with fewer mistakes. Irritating features do, however, crop up again such as the presentation of a sagittal MR image of the cranio-cervical region (Fig. 1D) in the conventional plane with

the nose to the reader's left, only to have the corresponding cadaveric section displayed in the opposite plane.

In summary, although the quality of the cadaveric sections is on the whole good, that of the MR images is of a lesser standard. In addition, there are rather too many textual mistakes, omissions and cases of confusing labelling. It is difficult to know at whom this atlas is aimed. There are now several MR atlases available. These are probably of superior quality and also in English, which in reality and in the absence of an excellent full translation, makes this book a less attractive proposition for a personal collection or departmental library.

T. JASPAN

Quality Assurance in Radiotherapy. Guide prepared following a workshop at Schloss Reinsburg Federal Republic of Germany 3-7 December 1984, pp. 52, 1988 (World Health Organization, Geneva), SFr 11; US\$6.60. ISBN 92-4-154224-1

This short guide was produced jointly by the Institute of Radiation Hygiene, Federal Republic of Germany and the World Health Organization, following a workshop held in December 1984. No doubt there is good reason for the 3 years or so delay in publishing but a concern for prospective purchasers must be whether the contents remain topical. But for a few minor exceptions, this does not seem to be a problem. For example, an effort has been made to bring up to date the reference list although the reference for the latest IAEA Code of Practice is not correct. Other minor criticisms, perhaps related to the age of the original text, are that no mention is made of the possibilities of on-line digital imaging during therapy for quality control. Neither do the authors believe that "at the present time it is possible either to encourage or discourage the use" of conventional treatment unit-linked verification systems. Surely this is a 1984 view? Such systems have been in use for so long now that it must be possible to say something positive (or even negative) on their effect on quality assurance.

These few reservations apart, the guide has a lot to recommend it. It makes concise and easy reading, yet it covers the broad spectrum of quality assurance procedures needed for consistent and accurate therapy. Following a brief introduction, the operational and organizational aspects of a quality assurance programme are discussed. It is interesting to note that the responsibility for establishing such a programme is laid firmly on the clinician in charge of the radiotherapy department. This I believe is correct. It is unfortunately all too common for quality assurance programmes to be merely tolerated rather than initiated and encouraged by clinical staff.

The physical and technical aspects including safety are dealt with in the main body of the report. Here the emphasis is on complete coverage rather than detailing procedures. Rather than generate alternatives of its own, where appropriate, the text summarizes and references the current standards and codes from such organizations as the IEC, IAEA, ICRP and ICRU.

The final section of the guide deals with clinical aspects of quality assurance procedures. The importance of reaching a consensus on "best current management" for a particular disease is stressed and ways in which this can be achieved by good clinical practice are identified. As with the earlier sections, the approach is comprehensive rather than detailed.

This guide is a straightforward and interesting read for everyone involved in quality assurance procedures in radiotherapy, including radiotherapists, physicists and radiographers. I would be surprised if many of us, giving the guide an hour or two of our attention, would not be provoked

into improving some aspects of quality assurance within our own departments.

G. D. LAMBERT

Radiopharmacy and Radiopharmacology Yearbook 2. Ed. by Peter H. Cox, pp. xii + 433, 1987 (Gordon and Breach, New York), \$85.00.
ISBN 2-88124-167-0

Many nuclear medicine personnel I know are for one reason or another "too busy". Most agree that it is a good idea to keep up to date with current developments and the *Radiopharmacy and Radiopharmacology Yearbooks* are welcome developments in this area.

As in Volume 1, Volume 2 is divided into three sections: the first section comprises a series of selected reviews of specific topics; the second is a series of selected literature citations from work that has been published during 1984/85; and the third section deals with new products and lists of manufacturers.

The review section commences with a chapter on radioactive particulates, and the author deals with methods of preparation, quality-control techniques and biokinetic data including much previously unpublished animal work. Also included are data on the comparative size of particulates, and a list of more than 200 references. The review represents the most informative that I have yet seen and should be essential reading for both radiopharmacists and clinicians.

The chapter on liposomes is particularly well written, and the methods of preparation, properties and clinical applications are clearly explained. Also discussed in detail are the advantages of liposomes over conventional radiopharmaceuticals, *i.e.* that they can be used to carry multiple markers, and that they can produce an altered biodistribution in order to image areas that are normally inaccessible. The disadvantages of liposomes are also described, *i.e.* their lack of success in targeting to organs other than the reticulo-endothelial system. Also emphasized is the fact that despite two decades of research into liposomes, clinical applications are at present few owing to their complexity of preparation. The explanations are accompanied by excellent schematic diagrams and electron micrographs.

Next comes a chapter on the clinical significance of impurities in clinical observations. The author examines retrospectively the results of 112 radiochemical analyses and investigates whether the results correlate with the clinical observations of a skilled observer. Although the text was sometimes difficult to comprehend as a result of poor data presentation and lack of proper paragraphing, the contents and conclusions are important to both pharmacists and clinicians.

The chapter entitled "Iodine-123 in nuclear medicine" describes the production of the isotope by various methods, as well as techniques of labelling ligands with iodine 123. Of particular importance is the section on imaging and counting in which the author describes various methods of improving image quality. Also included is a useful summary of the different compartmental models for iodine metabolism. The review is made complete by the excellent line diagrams of the production processes and the numerous graphs detailing the physical characteristics of the isotope.

The final review deals with gallium based radiopharmaceuticals. The author traces the history of this group of compounds and describes more than 10 gallium radiopharmaceuticals that have been in use since the 1960s. Also included is an abbreviated discussion on the use of positron-emitting isotopes of gallium. The chemical aspects of gallium are also touched upon including the author's own

important work in ascertaining the electrical charge on gallium complexes. In all, a useful chapter but I would have preferred a more expanded version of the section on gallium-based positron emitters.

The second section of the book contains selected abstracts and is arranged under subheadings, first relating to the functional organ and secondly relating to the radionuclide. Whilst the primary sources of information are from European or American journals, screening has been extended to other sources, for example the *Chinese Journal of Nuclear Medicine*. The opening set of abstracts deals with literature relating to the effect of patient medication on biodistribution and reflects the need for continual updating of information on this important topic. The remaining abstracts deal with papers pertaining to the cardiovascular, central nervous system, endocrine, gastrointestinal tract, haematological and locomotory systems.

The final section dealing with details of radiopharmaceutical manufacturers was, I felt, very useful although the UK offices of a number of European companies were not listed. It is to be hoped that future editions will include this information for the benefit of UK purchasers. Also missing was a list of forthcoming scientific meetings (the foreword specifically mentions the inclusion of this topic), and it is hoped that future volumes will contain this information.

A minor criticism of the book is the occasional poor grammar and spelling. Meticulous checking of the text is necessary in a camera-ready publication of this type. On one page, for example, there were six typographical or textual errors. Another criticism is the long-term interval (3 to 4 years) between publication of the selected abstracts and publication of the volume. For the book to be a true "state of the art" manual the time interval will need to be considerably reduced. However, the *Radiopharmacy and Radiopharmacology Yearbook* is well worth having, particularly for the review section, and at £17 (soft-back edition) represents excellent value for money. It is encouraging to note that the series is being expanded further to include broad topics of general nuclear medicine interest (a textbook of practical radiopharmacy is in the process of preparation), and future editions are awaited with great interest.

CHARLES B. SAMPSON

The Radiologist's First Reader. By Harry W. Fischer, pp. xii + 231, 1988 (BookCrafters, Chelsea, Michigan), \$18.95, obtained from Granville Medical Books, Ohio.

ISBN: Library of Congress Catalog Card No. 88-080218
This delightful small book is a highly personal collection of articles. The first grouping consists of radiologists' views of their practice and themselves from such venerable practitioners as Mellins, Newell, Goin, Sherman, Ross and Riggler. The history of Roentgen's laboratory over a span of 62 years is illustrated by three reflections. There then follows a group of dissertations on teaching from Sherman, Miller and Campbell with a characteristic Felson Editorial and a forceful reply to that Editorial from Cimmino. Next is a selection of poetry and cartoons laced with some satire. The final section consists of a eulogy of John Hodson and John Edward Campbell and an autobiographical sketch of Paul Hodges.

This is essentially a transatlantic text but this does not detract from its charm and interest. Ideal for pleasure reading on a rainy day or for the Christmas stocking. For the mechanically minded, there is even a radiograph of a jeep.

D. G. SHAW

1988 *Yearbook of Diagnostic Radiology*. Ed. by David G. Bragg, pp. 524, 1988 (Year Book Medical Publishers, Chicago), £35.50.

ISBN 0-8151-1137-1

Another year, another *Year Book*: 357 articles from nearly 700 publications, predominantly North American. Three of the six Associated Editors are new.

The familiar pattern of the publication remains in the diversity of the selected articles and is consistently satisfying. Editorial comments as usual embellish the abstracted articles. The series continues to justify loyal adherence.

The articles, however, no matter how well selected, are essentially disjointed and it will be interesting to see how the more carefully structured annual reviews, coming particularly from the West Coast, will rival the *Year Books* for our attention and money in the years to come. Meanwhile the series can continue to be recommended as an efficient method of keeping abreast of at least some of the ever expanding literature.

D. G. SHAW

Contemporary Issues in Computed Tomography. Computed Tomography of the Gastrointestinal Tract. Ed. by Elliott K. Fishman and Bronwyn Jones, pp. xi + 298, 1988 (Churchill Livingstone, New York), £40.00.

ISBN 0-443-08512-9

This series by Churchill Livingstone is very good and could be said to have "captured" this market. By focusing on one clinical area, here the gastrointestinal tract, the team of writers can produce an up-to-date account which usually surpasses those found in comprehensive textbooks. The danger is that too many such books appear and this particular issue competes directly with *Computed Tomography of the Gastrointestinal Tract, Including the Peritoneal Cavity and Mesentery* edited by Morton Meyers. Both are excellent; this volume is slightly cheaper!

The authors lined up here have produced interesting material and the editors should be congratulated on ensuring uniformity of style and avoiding undue repetition. The choice of topics is generally sound and realistic for British practice. Computed tomography (CT) of appendicitis does not feature here! Although abscesses are briefly covered in an excellent chapter on acute gastrointestinal abnormalities, the use of CT for these lesions might have been more extensive in view of their close connection to the gastrointestinal tract, particularly as there is a whole chapter on peritoneal metastases. The anatomy of upper abdominal abscesses is, however, well covered in the section on upper abdominal peritoneal spaces and ligaments. An astonishing pitfall is demonstrated in this section where a pseudoaneurysm mimics a liver abscess; by luck, rather than judgement, an angiogram was performed prior to percutaneous drainage! It was cheering to find that pseudomyxoma peritonei was comprehensively described although the authors here did not come down off the fence as to whether the term should or should not be reserved for the rare benign but locally recurrent condition. The section on colorectal cancer was very well written and the section on the correlation of CT and magnetic resonance imaging of the gastrointestinal tract was informative; there will be an increasing need for such comparisons over the next few years.

This book should be of use to all radiologists who have access to CT and the large number of gastroenterologists for whom CT is still a relatively new technique. The illustrations are of high quality and demonstrate the pertinent points. This

volume represents fair value for money. It is everything that one has come to expect from this high-quality series.

ADRIAN DIXON

ALAN FREEMAN

Diagnostic Imaging of the Liver, Biliary Tract and Pancreas. Data Analysis and Diagnostic Procedures. By S. Sakuma, T. Ishigaki and T. Takeuchi, pp. xii + 340, 1987 (Springer-Verlag, Berlin), DM 98.

ISBN 3-540-16667-X (Berlin)

0-387-16667-X (New York)

This is an intriguing book dedicated to diagnostic imaging of the liver, biliary tract and pancreas. As stated in the preface "the development and the widespread clinical application of various diagnostic imaging modalities, such as diagnostic ultrasonography, X-ray computed tomography, single photon emission computed tomography and magnetic resonance imaging have been beyond all expectation". Reading the book, however, your reviewer began to wonder if the authors had lost sight of the patient amidst their adulation of all these (relatively) new imaging methods.

The book is divided into two parts. The first is devoted to descriptions of the different imaging techniques from the plain abdominal radiograph to computed tomography (CT), angiography and direct cholangiography. This is excellent, being well referenced and illustrated, though of interest there is nothing on magnetic resonance, despite the preface. Normal anatomy is included within this section and again this is very comprehensive despite a lapse into French anatomical terms on page 92. Several details may be questioned, such as the value of testing for sensitivity to intravenous contrast media before CT (page 54) or endoscopic retrograde cholangiopancreatography (ERCP) (page 143), and likewise the wisdom of giving a combined dose of oral and intravenous cholecystographic contrast media to opacify the biliary tree (page 136) is debatable.

The second section of the book is then devoted to individual case reports. Liver tumours, abscess and injury are all illustrated together with biliary and pancreatic disease. It is this section in particular that gives rise to the impression that the authors have gone to a great deal of effort to produce many beautiful illustrations of different diagnostic tests, without wholly considering if they are of direct benefit to the patient. The reader is guided through these tests by a number of somewhat complicated flow diagrams, but is left wondering if it is really of benefit to perform angiography in cases of liver abscess (page 193) or primary sclerosing cholangitis (page 259).

Despite these points there is no doubt that this is a highly comprehensive and lavishly illustrated book on hepatobiliary imaging. It is also good value at DM 98 but more suitable for library rather than individual purchase.

A. FREEMAN

Two-dimensional Echocardiographic Atlas. Volume 1. Congenital Heart Disease. By J. B. Seward, A. J. Tajik, W. D. Edwards and D. J. Hagler, pp. xiv + 598, 1987 (Springer-Verlag, New York), DM 390.

ISBN 0-387-96473-8 (New York)

3-540-96473-8 (Berlin)

This book is a beautifully produced and illustrated atlas which fulfils the promise that one might expect from such distinguished authors. Volume 1 reviewed here is devoted to congenital heart disease and this has been covered as comprehensively as anyone might wish.

The majority of the book consists of two-dimensional echocardiographic illustrations with accompanying M-mode and Doppler traces, cardiac angiograms, line drawings and pathological illustrations where appropriate.

The difficulties of representing the moving two-dimensional scan in selected still frames are well known, but this book has been very successful in this respect. Good illustrations of straightforward typical abnormalities have been included as well as examples of very unusual abnormalities of connection or function.

The illustrations are accompanied by a short descriptive text on each page and of particular value is the "imaging note" included with most illustrations. This reflects the practical experience of the authors and will no doubt be of much help to those trying to emulate these high-quality scans.

Another particularly strong point of the book is the high quality of the pathological specimens that have been illustrated. These have been beautifully sectioned and where appropriate they clarify the echocardiographic images in a very helpful way.

As would be expected, each chapter concludes with a comprehensive selection of references for further reading.

The only daunting aspect of this book is its comprehensive nature. It certainly cannot be read from beginning to end but should be used as an authoritative textbook to be kept in the department where scanning is undertaken. As with all such books it is a little expensive but I feel that it is an essential reference work for any department undertaking paediatric echocardiography.

PETER WILDE

Fetal Echocardiography. An Atlas. By Kathryn L. Reed, Caroline F. Anderson and Lewis Shenker, pp. viii + 138, 1988 (Alan R. Liss, New York), \$62.50.
ISBN 0-8451-4250-X

Fetal echocardiography is gradually evolving and becoming more widely used and this atlas sets out to indicate the status of the technique at present. The introduction lists those patients for whom the technique is most appropriate and points out some of the conditions that cannot be excluded by the technique. A chapter follows on fetal heart anatomy and physiology with an extensive chapter on the methods of examination. The second half of the book is devoted to the abnormal fetal heart, and the book is completed with short sections on M-mode cardiography, colour flow mapping and Doppler ultrasound. The authors make the subject more complicated using a nomenclature relating the fetal heart position to the position of the fetus and of the fetus within the mother, which is both unnecessary and confusing. This is compounded by the nomenclature for the position of the fetus in the mother being non-standard, with the maternal lower abdomen to the left of the picture rather than the right and the patient's right on the right of the picture.

There are a number of errors including the interventricular septum being called the intraventricular septum (page 12). On page 30 it is stated that valvular insufficiency can be excluded on the appearances of the heart and this is not entirely true. The old nomenclature of univentricular heart is used (page 54) and this is rather confusing. It is rather disappointing that the authors make no comment of how different the cardiac structures, in particular the ventricular wall thicknesses and septal thickness, look with the fetal heart in different orientations, although this is demonstrated on several pictures without comment. The section on colour flow mapping assumes a greater level of knowledge than the remainder of the

book but is very valuable with some informative colour illustrations demonstrating the value of this rapidly developing technique.

The standard of production of the book is excellent and the authors are to be commended for the most excellent medical illustrations that accompany the ultrasound pictures. In spite of the criticisms, this book is a valuable up-to-date review of the subject which will be of interest to those involved in obstetric ultrasound, and considering the quality of the illustrations is very good value for money. It should certainly be available in any department undertaking fetal echocardiography.

D. W. PILLING

Obstetrical Measurements in Ultrasound. A Reference Manual. By Alfred B. Kurtz and Barry B. Goldberg, pp. xii + 214, 1988 (Year Book Medical Publishers, Chicago), £34.00.
ISBN 0-8151-5222-1

The authors have taken the data from most if not all the papers published on measurements in obstetrical ultrasound, and have critically analysed them. In some cases it has been necessary to reorganize the presentation of the data to give a consistent format and to enable some comparison of the value of the various papers. This book is organized into three parts, the first covering first trimester obstetric measurements, second covering the second and third trimester measurements and a small final section covering multiple gestations. The largest section, the middle one, is further subdivided into head measurements, body measurements, combined head and body measurements and uterine measurements. For each parameter, the papers on the subject are analysed, criticized for their scientific method or conclusion and in most cases a recommendation made as to which method of measurement or set of figures is most appropriate for everyday use.

The authors have succeeded entirely in producing a most readable book out of a subject which at first sight would seem rather "dry". The references are extremely comprehensive and up to date, and will have something to offer to even the most experienced person in the field of obstetric ultrasound. It would be of great interest to those taking the Diploma in Medical Ultrasound but covers far more ground than is necessary for this examination. This book is likely to become a standard work and will certainly be found on the bookshelves of every obstetric ultrasound department in due course.

D. W. PILLING

Cranial Magnetic Resonance Imaging. By Allen D. Elster, pp. xii + 423, 1988 (Churchill Livingstone, New York), £75.00.
ISBN 0-443-08542-0

In the preface to this book, Dr Elster comments that at the time it was written there was no available textbook devoted exclusively to cranial magnetic resonance imaging (MRI) and that he wished to distinguish established fact from opinion and uncorroborated data. There are now numerous textbooks available devoted to cranial imaging so how does this book differ from the others and has the author achieved his aim?

The book is divided into 12 chapters, the first two consisting of the physical and technical parameters of MRI and the third and fourth being devoted to normal cranial anatomy and the congenital and developmental anomalies encountered. Chapters 5 to 12 deal with specific disease processes of the cranial cavity, skull base and orbit. This is followed by a relatively limited glossary and the book ends with a further

section of normal anatomy in the three orthogonal planes, which to some extent complements Chapter 3. The items of pathology mentioned in each of the chapters cover most of the recognized pathological conditions. The bulk of the text, however, is clinico-pathological with extensive descriptions of each condition and much of the imaging devoted to the appearances on computed tomography (CT). In only selected areas are the appearances on MRI explored in any depth. The chapter dealing with haemorrhage is a useful review of a difficult subject but all too often little direct advice is given to the reader as to which of the two, CT or MRI, should be undertaken in a given condition.

The book reads clearly and the illustrations are well positioned in the text, providing additional information. There is little, if any, repetition in the text, which is to be expected in a single-author work and apart from a few minor but rather annoying spelling mistakes it is in general quite well laid out. The quality of the illustrations is rather variable; some are quite poor although they are at least adequate for their purpose and the labelling is satisfactory.

Unfortunately at 423 pages including the index, this is not a small book and naturally its price (£75 sterling) reflects this. The main criticism that I have of the book is that there is, despite its title, relatively little pure MRI data and nor does it place MRI in perspective. The content could easily have been reduced by 50% without much loss and this would have undoubtedly reduced its cost. There are a number of similar books now available which provide rather better and more coherent MRI information and I do not really believe that this has satisfactorily fulfilled the author's objective as set out in the preface. If this is to be the reader's only book on MRI, I cannot recommend it but no doubt it will find its way into libraries if only because the bibliography is extensive.

D. P. E. KINGSLEY

Colour Blood Flow Imaging of the Heart. By Dierk A. Redel, pp. vii + 130, 1988 (Springer-Verlag, Berlin), DM 298. ISBN 3-540-16521-5 (Berlin) 0-387-16521-5 (New York)

In this rather slim book, Dr Redel aims to provide an introduction to the rapidly developing field of colour blood-flow imaging of the heart. The book is divided into three sections, starting with an introduction to the physical principles of colour blood-flow imaging and the artefacts that can occur. This is followed by a section on normal appearances and concludes with a section on pathological appearances. The initial description of the principles of blood-flow imaging and the production of artefacts is the weakest part of the book. In his introduction the author states this section has been kept short as relatively little information is available to give a comprehensible introduction to the reader who is not already familiar with the technique. This is not true. The introduction

is rather confusing and either needs to be longer and clearer or should be removed altogether. Some parts of this first section are really only understandable to someone who already understands the physical principles of colour blood-flow imaging.

The section dealing with the normal appearances is rather more satisfactory and the long final section dealing with pathological appearances is good. The author deals with a large number of the commoner congenital and acquired cardiac abnormalities that produce flow anomalies which are suitable for investigation by colour blood-flow imaging. The illustrations and the explanatory text are, for the most part, of a good standard when explaining pathological appearances. However, there are a number of images where, in spite of the author's stated opinion that illustrative drawings are now necessary, it is very difficult to understand what is being illustrated and in a few cases the legends to the figures are potentially confusing. There are a number of images, particularly in the early part of the book, where the physical principles and artefacts of colour flow imaging are being illustrated, which would have benefited from explanatory diagrams. The lack of clarity of these few illustrations seems to relate more to the quality of the original image rather than to the standard of reproduction which throughout the book is good. All the illustrations are in colour and most are well labelled.

The early section of the book suffers in places from a rather difficult style of English and this is particularly apparent when the author is trying to explain some of the physical principles involved. Later in the book, when dealing with pathological conditions, the style of the English improves and is much less complicated. This book is said to be aimed at the reader who has experience in two-dimensional echocardiography and also has some understanding of the principles of Doppler ultrasound. I think that the author has assumed that the knowledge of Doppler is high and he is presumably aiming this book at those people who have considerable experience in conventional Doppler and two-dimensional echocardiography and are about to start using colour blood-flow imaging equipment.

Currently, this book is up to date but in a rapidly advancing field I suspect that it will soon be superseded by more up-to-date and comprehensive texts that will no doubt appear over the next few years. Over the years the publishers will have to overcome the apparently considerable problem of cost in reproducing large numbers of colour illustrations. With a current price in the region of £92 the book seems to be extremely expensive for what it contains and its purchase by any individual cannot be recommended. It may have a place as an initial textbook in the library of the departments where colour blood-flow imaging is currently being introduced. However, at this price, with only 118 useful pages of text and 211 illustrations, it cannot be regarded as good value.

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